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FILE COVERS 1907 - 15 Jul 2009 VOL 151 ISS 3
FILE LAST UPDATED: 14 Jul 2009 (20090714/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Apr 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Apr 2009

HCAplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2009.

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This file contains CAS Registry Numbers for easy and accurate substance identification.

The ALL, BIB, MAX, and STD display formats in the CA/CAplus family of databases will soon be updated to include new citing references information. This enhancement may impact record import into database management software. For additional information, refer to NEWS 22.

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

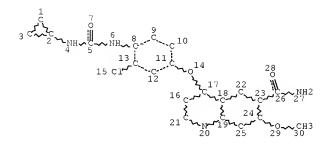
GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 30

STEREO ATTRIBUTES: NONE

L3 107 SEA FILE=REGISTRY SSS FUL L1

L4 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 30

STEREO ATTRIBUTES: NONE

L5 14 SEA FILE=REGISTRY SUB=L3 SSS FUL L4
L6 26 SEA FILE=HCAPLUS ABB=ON PLU=ON L5

L7 20506 SEA FILE=HCAPLUS ABB=ON PLU=ON ("SMALL-CELL LUNG CARCINOMA"/C

V OR "CARCINOMA (L) PULMONARY SMALL-CELL"/CV OR "LUNG (L) SMALL-CELL CARCINOMA"/CV OR "LUNG, NEOPLASM (L) SMALL-CELL CARCINOMA"/CV OR "LUNG OAT CELL CARCINOMA"/CV OR "LUNG SMALL CELL CARCINOMA"/CV OR "SMALL CELL CARCINOMA"/CV OR "SMALL CELL LUNG CANCER"/CV OR "SMALL LUNG CELL CARCINOMA"/CV OR "SMALL-CELL CARCINOMA (LUNG)"/CV OR "SMALL-CELL CARCINOMA (PULMONARY)"/CV

) OR SMALL(L)CELL(L)LUNG(L)(CANCER? OR CARCINOMA)

L8 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L6 AND L7

=> d ibib abs hitstr 18 1-4

L8 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2009:583215 HCAPLUS Full-text

DOCUMENT NUMBER: 150:506980

TITLE: Combination of anti-angiogenic substance and

anti-tumor platinum complex

INVENTOR(S): Yamamoto, Yuji

PATENT ASSIGNEE(S): Eisai R & D Management Co., Ltd., Japan

SOURCE: PCT Int. Appl., 97pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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	WO 2009060945					_	 2009	 0514	WO 2008-JP70321						20081107		
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		CF	, СН,	CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DO,	DZ,	EC,	EE,	EG,	ES,
		FI	, GB,	GD,	GE,	GH,	GM,	GT,	HN,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,
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		ΑN	, AZ,	BY,	KG,	ΚZ,	MD,	RU,									
PRIORITY APPLN, INFO.: US 2007-986641P P 20071109											109						
OTHER SOURCE(S): MARPAT 150:506980																	
AB The object is to discover a pharmaceutical composition having an excellent																	
	anti-tumor effect and a therapeutic method for cancer. 4-(3-Chloro-4-																
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RN 417716-92-8 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy- (CA INDEX NAME)

RN 417719-50-7 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-[[[[(1R,2S)-2-

fluorocyclopropyl]amino]carbonyl]amino]phenoxy]-7-methoxy-, rel- (CA
INDEX NAME)

Relative stereochemistry.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2008:1065363 HCAPLUS Full-text

DOCUMENT NUMBER: 150:297980

DOCUMENT NUMBER: 130:29/900

TITLE: Multi-Kinase Inhibitor E7080 Suppresses Lymph Node and

Lung Metastases of Human Mammary Breast Tumor MDA-MB-231 via Inhibition of Vascular Endothelial Growth Factor-Receptor (VEGF-R) 2 and VEGF-R3 Kinase

AUTHOR(S): Matsui, Junji; Funahashi, Yasuhiro; Uenaka,

Toshimitsu; Watanabe, Tatsuo; Tsuruoka, Akihiko;

Asada, Makoto

CORPORATE SOURCE: Discovery Research Laboratories II, Eisai Co. Ltd.,

Tokodai, Tsukuba, Japan

SOURCE: Clinical Cancer Research (2008), 14(17), 5459-5465

CODEN: CCREF4; ISSN: 1078-0432

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal LANGUAGE: English

PURPOSE: Vascular endothelial growth factor (VEGF)-C/VEGF-receptor 3 (VEGF-R3) AB signal plays a significant role in lymphangiogenesis and tumor metastasis based on its effects on lymphatic vessels. However, little is known about the effect of inhibiting VEGF-R3 on lymphangiogenesis and lymph node metastases using a small-mol. kinase inhibitor. Exptl. Design: We evaluated the effect of E7080, a potent inhibitor of both VEGF-R2 and VEGF-R3 kinase, and bevacizumab on lymphangiogenesis and angiogenesis in a mammary fat pad xenograft model of human breast cancer using MDA-MB-231 cells that express excessive amts. of VEGF-C. Lymphangiogenesis was determined by lymphatic vessel d. (LVD) and angiogenesis by microvessel d. (MVD). RESULTS: In contrast to MDA-MB-435 cells, which expressed a similar amount of VEGF to MDA-MB-231 calls with an undetectable amount of VEGF-C, only MDA-MB-231 exhibited lymphangiogenesis in the primary tumor. E7080 but not bevacizumab significantly decreased LVD within the MDA-MB-231 tumor. E7080 and bevacizumab decreased MVD in both the MDA-MB-231 and MDA-MB-435 models. E7080 significantly suppressed regional lymph nodes and distant lung metastases of MDA-MB-231, whereas bevacizumab significantly inhibited only lung metastases. E7080 also decreased both MVD and LVD within the metastatic nodules at lymph nodes after resection of the primary tumor. CONCLUSIONS: Inhibition of VEGF-R3 kinase with E7080 effectively decreased LVD within MDA-MB-231 tumors, which express VEGF-C. Simultaneous inhibition of both VEGF-R2 and VEGF-R3 kinases by E7080 may be a promising new strategy to control regional lymph node and distant lung metastases.

IT 417716-92-8

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(E 7080; dual tyrosine kinase inhibitor of VEGF-R2 and VEGF-R3, E7080 decreased lymphangiogenesis, angiogenesis, lymph node and lung metastasis in human breast cancer cell xenografted into mouse)

RN 417716-92-8 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

28

[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy- (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2009 ACS on STN
1.8
ACCESSION NUMBER:
                        2008:14364 HCAPLUS Full-text
DOCUMENT NUMBER:
                         148:253561
TITLE:
                         E7080, a novel inhibitor that targets multiple
                         kinases, has potent antitumor activities against stem
                         cell factor producing human small cell lung
                         cancer H146, based on angiogenesis inhibition
                         Matsui, Junji; Yamamoto, Yuji; Funahashi, Yasuhiro;
AUTHOR(S):
                         Tsuruoka, Akihiko; Watanabe, Tatsuo; Wakabayashi,
                         Toshiaki; Uenaka, Toshimitsu; Asada, Makoto
                         Tsukuba Research Laboratories, Tsukuba, Ibaraki,
CORPORATE SOURCE:
                         300-2635, Japan
SOURCE:
                         International Journal of Cancer (2007), Volume Date
                         2008, 122(3), 664-671
                         CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER:
                         Wilev-Liss, Inc.
DOCUMENT TYPE:
                        Journal
LANGUAGE:
                        English
     E7080 is an orally active inhibitor of multiple receptor tyrosine kinases
     including VEGF, FGF and SCF receptors. In this study, we show the inhibitory
     activity of E7080 against SCF-induced angiogenesis in vitro and tumor growth
     of SCF-producing human small cell lung carcinoma H146 cells in vivo. E7080
     inhibits SCF-driven tube formation of HUVEC, which express SCF receptor, KIT
     at the IC50 value of 5.2 nM and it was almost identical for VEGF-driven one
     (IC50 = 5.1 \text{ nM}). To assess the role of SCF/KIT signaling in tumor
     angiogenesis, we evaluated the effect of imatinib, a selective KIT kinase
     inhibitor, on tumor growth of H146 colls in nude mice. Imatinib did not show
     the potent antitumor activity in vitro (IC50 = 2,200 nM), because H146 cells
     did not express KIT. However, oral administration of imatinib at 160 mg/kg
     clearly slowed tumor growth of H146 cells in nude mice, accompanied by
     decreased microvessel d. Oral administration of E7080 inhibited tumor growth
     of H146 cells at doses of 30 and 100 mg/kg in a dose-dependent manner and
     caused tumor regression at 100 mg/kg. While anti-VEGF antibody also slowed
     tumor growth, it did not cause tumor regression. These results indicate that
     KIT signaling has a role in tumor angiogenesis of SCF-producing H146 cells,
     and E7080 causes regression of H146 tumors as a result of antiangiogenic
     activity mediated by inhibition of both KIT and VEGF receptor signaling.
     E7080 may provide therapeutic benefits in the treatment of SCF-producing
     tumors.
     417716-92-8
ΤТ
     RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (E 7080; E7080, a novel inhibitor that targets multiple kinases, has
       potent antitumor activities against stem cell factor
       producing human small cell lung
        cancer H146, based on angiogenesis inhibition)
     417716-92-8 HCAPLUS
CN
     6-Quinolinecarboxamide, 4-[3-chloro-4-
```

[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy- (CA INDEX NAME)

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2004:780539 HCAPLUS Full-text

DOCUMENT NUMBER: 141:289013

TITLE: c-Kit kinase inhibitor

INVENTOR(S): Yamamoto, Yuji; Watanabe, Tatsuo; Okada, Masayuki;

Tsuruoka, Akihiko

PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan SOURCE: PCT Int. Appl., 28 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA'	TENT :	KIN	D	DATE				ICAT:		DATE								
WO	WO 2004080462					A1 20040923												
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		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	NA,	NI,	
		NO,	ΝZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	
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		BY,	KG,	KΖ,	MD,	RU,	ТJ,	TM,	ΑT,	ΒE,	ВG,	CH,	CY,	CZ,	DE,	DK,	EE,	
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		SK,	TR,	BF,	ΒJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,	
		TD,	ΤG															
US	2004	0253	205		A1		2004	1216		US 2	004-	79791	20040310					
EP	1604	665			A1		2005	1214		EP 2	004-	7190	54		2	0040	310	
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		ΙE,	SI,	LT,	LV,	FΙ,	RO,	MK,	CY,	ΑL,	TR,	BG,	CZ,	EE,	HU,	PL,	SK	
PRIORIT:	Y APP	LN.	INFO	.:						JP 2	003-	62823	3	A 20030310				
									JP 2003-302803					A 20030827				
										WO 2004-JP3087					W 20040310			
OTHER S	MARPAT 141:289013																	

GΙ

$$\mathbb{R}^{2}$$

AB It is found out that a compound represented by the following general formula I (R1 = Me, etc.; R2 = cyano, etc.; R3 = H, etc.; and R4 = H, etc.) shows a potent c-Kit kinase inhibitory activity and suppresses the proliferation of cancer cells activated by c-Kit kinase both in vitro and in vivo. Thus, a novel anticancer agent showing a c-Kit kinase inhibitory activity is found out.

IT 417716-92-8, 4-(3-Chloro-4-

((cyclopropylaminocarbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(c-Kit kinase inhibitor)

RN 417716-92-8 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy- (CA INDEX NAME)

REFERENCE COUNT:

9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

 \Rightarrow \Rightarrow d stat que 111 L1 STR

NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES: RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 30

STEREO ATTRIBUTES: NONE

L3 107 SEA FILE=REGISTRY SSS FUL L1 L4 STR

NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 30

STEREO ATTRIBUTES: NONE

L5 14 SEA FILE=REGISTRY SUB=L3 SSS FUL L4 L6 26 SEA FILE=HCAPLUS ABB=ON PLU=ON L5

L7 20506 SEA FILE=HCAPLUS ABB=ON PLU=ON ("SMALL-CELL LUNG CARCINOMA"/C
V OR "CARCINOMA (L) PULMONARY SMALL-CELL"/CV OR "LUNG (L)
SMALL-CELL CARCINOMA"/CV OR "LUNG, NEOPLASM (L) SMALL-CELL
CARCINOMA"/CV OR "LUNG OAT CELL CARCINOMA"/CV OR "LUNG SMALL
CELL CANCER"/CV) OR ("SMALL CELL CARCINOMA"/CV OR "SMALL CELL

LUNG CANCER"/CV OR "SMALL LUNG CELL CARCINOMA"/CV OR "SMALL-CEL

L CARCINOMA (LUNG)"/CV OR "SMALL-CELL CARCINOMA (PULMONARY)"/CV
) OR SMALL(L)CELL(L)LUNG(L) (CANCER? OR CARCINOMA)

L8 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L6 AND L7

L9 22 SEA FILE=HCAPLUS ABB=ON PLU=ON L6 NOT L8

L10 18 SEA FILE=HCAPLUS ABB=ON PLU=ON L9 AND (?CANCER? OR ?CARCIN?
OR ?TUMOR? OR ?MALIG? OR ?MEOPLAS?)

L11 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L10 AND (LUNG OR PULMON?)

=> d ibib abs hitstr 111 1-6

L11 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2007:863627 HCAPLUS Full-text

DOCUMENT NUMBER: 147:235192

TITLE: Preparation of urea derivatives containing nitrogenous aromatic ring compounds as inhibitors of angiogenesis

INVENTOR(S): Funahashi, Yasuhiro; Tsuruoka, Akihiko; Matsukura, Masayuki; Haneda, Toru; Fukuda, Yoshio; Kamata, Junichi; Takahashi, Keiko; Matsushima, Tomohiro;

Miyazaki, Kazuki; Nomoto, Ken-Ichi; Watanabe, Tatsuo; Obaishi, Hiroshi; Yamaguchi, Atsumi; Suzuki, Sachi; Nakamura, Katsuji; Mimura, Fusayo; Yamamoto, Yuji; Matsui, Junji; Matsui, Kenji; Yoshiba, Takako; Suzuki,

Yasuyuki; Arimoto, Itaru

PATENT ASSIGNEE(S): Eisai Co., Ltd, Japan

SOURCE: U.S., 458pp., Cont.-in-part of Appl. No.

PCT/JP01/09221. CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.							APPLICATION NO.											
US 7253286				B2 20070807								20030418						
US	2004	0053	908		A1 20040318													
WO	70 2002032872				A1	20020425				WO 2	001-	JP92		20011019				
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		NL,													_			
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CN 101029022	A	20070905	CN	2007-10007097		20011019
ES 2282299	Т3	20071016	ES	2001-976786		20011019
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US 20060160832	A1	20060720	US	2006-347749		20060203
AU 2006203099	A1	20060810	AU	2006-203099		20060719
AU 2006236039	A1	20061207	AU	2006-236039		20061116
AU 2006236039	B2	20080522				
PRIORITY APPLN. INFO.:			JP	2000-320420	A	20001020
			JP	2000-386195	Α	20001220
			JP	2001-46685	Α	20010222
			WO	2001-JP9221	A2	20011019
			AU	2001-295986	A3	20011019
			AU	2001-95986	TO	20011019
			CN	2001-819710	A3	20011019
			EP	2001-976786	A3	20011019
			JP	2002-536056	A3	20011019
			US	2003-420466	A3	20030418
			US	2005-293785	A1	20051202
		- 4 45 005460				

OTHER SOURCE(S): MARPAT 147:235192

AB N-aryl or N-heteroarylurea derivs. represented by the general formula Ag-Xg-Yg-Tg1 or salts thereof, or hydrates of both [wherein Ag = (un)substituted C6-14 aryl or 5- to 14-membered heterocyclic group; Xg = single bond, O, S, C1-6 alkylene, SO, SO2, (un)substituted NH; Yg = (un)substituted C6-14 aryl, 5- to 14-membered heterocyclic group, C1-8 alkyl, C3-8 alicyclic hydrocarbyl, C6-14 aryl-C1-6 alkyl, 5- to 14-membered heteroaryl-C1-6 alkyl, (CH2)gSO2 (g = 1-8), (CH2) faCH:CH(CH2) fb (fa, fb = 0, 1,2,3), etc.; and Tg1 = a group of the general formula -Eg-CO-NRg1(Zg) or Q; wherein Eg = a single bond, (un) substituted NH; Rg1 = H, (un) substituted C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C3-8 aliphatic hydrocarbyl, etc.; Zq = C1-8 alkyl, C3-8 alicyclic hydrocarbyl, C6-14 aryl, etc.; Zg1, Zg2 = (a) a single bond, (b) C1-6 alkylene optionally having ≥ 1 atoms selected from O, S, and N in the middle or the terminus of the chain and optionally substituted with oxo, (c) (un)substituted C2-6 alkenyl] are prepared These compds. are also inhibitors of vascular endothelial growth factor receptor kinase (VEGFR2 kinase) and are useful as antitumor agents against hemangioma, pancreatic cancer, stomach cancer, colon cancer, breast cancer, prostate cancer, lung cancer, brain tumor, leukemia, or ovarian cancer, as cancer metastasis inhibitors, and for the treatment of retina neovascularization, diabetic retinopathy, atherosclerosis, or inflammatory diseases such as osteoarthritis, rheumatoid arthritis, psoriasis, or delayed hypersensitivity. Thus, to solution of 334 mg 4-[6-(4benzyloxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenylamine in 4 mL DMF were added 0.066 mL pyridine and 0.102 mL Ph chlorocarbonate and stirred at room temperature for 2.5 h to give 330 mg N-[4-[6-(4-benzyloxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-

pyrrolo[2,3-d]pyrimidin-4-yloxy]-2- chlorophenyl]-N'-cyclopropylurea which (260 mg) was hydrogenolyzed over platinum oxide in ethanol overnight to give 160 mg N-[4-[6-(4-hydroxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenyl]-N'-cyclopropylurea (I). I showed IC50 of 0.02 nM for inhibiting the vascular endothelial growth factor (VEGF)-stimulated sandwich tube formation in vascular endothelial cell. 417716-92-3F 417719-50-7F

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of urea derivs. containing nitrogenous aromatic ring compds.

as

CN

TT

angiogenesis inhibitors for prevention or treatment of diseases)

RN 417716-92-8 HCAPLUS

6-Quinolinecarboxamide, 4-[3-chloro-4-

[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy- (CA INDEX NAME)

RN 417719-50-7 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-[[[[(1R,2S)-2-fluorocyclopropyl]amino]carbonyl]amino]phenoxy]-7-methoxy-, rel- (CA INDEX NAME)

Relative stereochemistry.

$$\begin{array}{c|c} \text{MeO} & \text{N} & \text{N} \\ \text{H2N} & \text{N} & \text{N} & \text{R} & \text{S} & \text{F} \\ \hline \\ \text{C1} & \text{N} & \text{R} & \text{S} & \text{F} \\ \end{array}$$

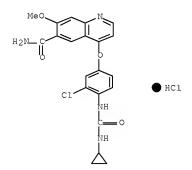
REFERENCE COUNT:

117 THERE ARE 117 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L11 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:1354247 HCAPLUS <u>Full-text</u>
DOCUMENT NUMBER:
                        146:100576
TITLE:
                        Preparation of amorphous salts of
                        4-[3-chloro-4-
                        [(cyclopropylaminocarbonyl)amino]phenoxy]-7-methoxy-6-
                        quinolinecarboxamide as antitumor agents
INVENTOR(S):
                        Sakaguchi, Takahisa; Tsuruoka, Akihiko
PATENT ASSIGNEE(S):
                        Eisai R & D Management Co., Ltd., Japan
                        PCT Int. Appl., 49pp.
SOURCE:
                        CODEN: PIXXD2
DOCUMENT TYPE:
                        Patent
LANGUAGE:
                        Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
    PATENT NO.
                       KIND DATE
                                       APPLICATION NO.
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                        A1 20061228 WO 2006-JP312487
                                                                 20060622
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            GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
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             SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG,
            US, UZ, VC, VN, ZA, ZM, ZW
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A1 20080305
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                                           US 2005-693044P P 20050623
WO 2006-JP312487 W 20060622
PRIORITY APPLN. INFO.:
AB
     This invention pertains to a method for producing amorphous salts of 4-[3-
     chloro-4-[(cyclopropylaminocarbonyl)amino]phenoxy]-7-methoxy-6-
     quinolinecarboxamide. The title compds. are useful as antitumor agents for
     various cancers, such as pancreas cancer, stomach cancer, colon cancer, breast
     cancer, prostate cancer, lung cancer, renal cancer, brain cancer, blood
     cancer, ovarian cancer, and hemangioma (no data).
     417716-92-8P
IΤ
     RL: PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN
     (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
     PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
        (drug candidate; preparation of salts of
        4-[3-chloro-4-[(cyclopropylaminocarbonyl)amino]phenoxy]-7-methoxy-6-
       quinolinecarboxamide as antitumor agents)
    417716-92-8 HCAPLUS
RN
```

CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy- (CA INDEX NAME)

ΙT 857890-31-4P 857890-33-6P 857890-35-8P 857890-37-0P 857890-39-2P 857890-41-6P 857890-45-0P 857890-47-2P 917572-43-1P 917572-44-29 RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (drug candidate; preparation of salts of 4-[3-chloro-4-[(cyclopropylaminocarbonyl)amino]phenoxy]-7-methoxy-6quinolinecarboxamide as antitumor agents) RN 857890-31-4 HCAPLUS CN 6-Quinolinecarboxamide, 4-[3-chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-, hydrochloride (1:1) (CA INDEX NAME)



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RN 857890-33-6 HCAPLUS
CN 6-Quinolinecarboxamide, 4-[3-chloro-4-
[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-, hydrobromide (1:1)
(CA INDEX NAME)
```

RN 857890-35-8 HCAPLUS
CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-,
4-methylbenzenesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 417716-92-8 CMF C21 H19 C1 N4 O4

CM 2

CRN 104-15-4 CMF C7 H8 O3 S

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857890-37-0 HCAPLUS
RN
CN
                  6-Quinolinecarboxamide, 4-[3-chloro-4-
                           [[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-, sulfate (1:1) (CA
                           INDEX NAME)
                           CM
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                           CRN 417716-92-8
                           CMF C21 H19 C1 N4 O4
      H2N-
                           CM
                           CRN 7664-93-9
                           CMF H2 O4 S
RN
                           857890-39-2 HCAPLUS
CN
                           6-Quinolinecarboxamide, 4-[3-chloro-4-
                            \hbox{\tt [[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-, methane sulfon a temperature of the control of th
                            (1:1) (CA INDEX NAME)
                           CM
                                                1
                           CRN 417716-92-8
                           CMF C21 H19 C1 N4 O4
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CM 2

CRN 75-75-2 CMF C H4 O3 S

CM :

CRN 417716-92-8 CMF C21 H19 C1 N4 O4

RN 857890-45-0 HCAPLUS
CN 6-Quinolinecarboxamide, 4-[3-chloro-4 [[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-, acetate
 methanesulfonate (1:?:?) (CA INDEX NAME)

CM 1

CRN 417716-92-8 CMF C21 H19 C1 N4 O4

CRN 75-75-2 CMF C H4 O3 S

CM 3

CRN 64-19-7 CMF C2 H4 O2

RN 857890-47-2 HCAPLUS

CN Ethanesulfonic acid, compd. with 4-[3-chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-6quinolinecarboxamide (1:1) (CA INDEX NAME)

CM 1

CRN 417716-92-8 CMF C21 H19 C1 N4 O4

CM 2

CRN 594-45-6 CMF C2 H6 O3 S

RN 917572-43-1 HCAPLUS
CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-, methanesulfonate, compd. with 1,1'-sulfinylbis[methane] (1:1:?) (CA INDEX NAME)

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CRN 417716-92-8
CMF C21 H19 C1 N4 O4
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CM 2

CRN 75-75-2

CMF C H4 O3 S

CM 3

CRN 67-68-5

CMF C2 H6 O S

RN CN 917572-44-2 HCAPLUS
6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-, ethanesulfonate, compd. with 1,1'-sulfinylbis[methane] (1:1:?) (CA INDEX NAME)

CM 1

CRN 417716-92-8 CMF C21 H19 C1 N4 O4

CM 2

CRN 594-45-6 CMF C2 H6 O3 S

CM 3

CRN 67-68-5 CMF C2 H6 O S

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2006:268466 HCAPLUS Full-text

DOCUMENT NUMBER: 144:324798

TITLE: Simultaneous use of sulfonamide-containing compound

and angiogenesis inhibitor

INVENTOR(S): Owa, Takashi; Ozawa, Yoichi; Semba, Taro

PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan SOURCE: PCT Int. Appl., 270 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

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PATENT NO.
                       KIND DATE
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                                                                DATE
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                                           WO 2005-JP17238
                                                             W 20050913
                                           WO 2006-JP4208
                                                             W 20060228
                        MARPAT 144:324798
OTHER SOURCE(S):
AB
     combined with an angiogenesis inhibitor.
```

- A pharmaceutical composition comprising a sulfonamide-containing compound
- IT 417716-92-8, 4-(3-Chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-

7-methoxy-6-quinolinecarboxamide 417719-50-7

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(sulfonamide-containing compds. and angiogenesis inhibitors for combination chemotherapy of cancer)

- RN 417716-92-8 HCAPLUS
- CN 6-Quinolinecarboxamide, 4-[3-chloro-4-
 - [[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy- (CA INDEX NAME)

RN 417719-50-7 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-[[[[(1R,2S)-2-

fluorocyclopropyl]amino]carbonyl]amino]phenoxy]-7-methoxy-, rel- (CA INDEX NAME)

Relative stereochemistry.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2005:612258 HCAPLUS Full-text

DOCUMENT NUMBER: 143:120562

TITLE: Crystal of salt of

4-[3-chloro-4-(cyclopropylaminocarbonyl)amino-phenoxy]-

7-methoxy-6-quinolinecarboxamide or solvate thereof

and processes for producing these

INVENTOR(S): Matsushima, Tomohiro; Nakamura, Taiju; Yoshizawa,

Kazuhiro; Kamada, Atsushi; Ayata, Yusuke; Suzuki, Naoko; Arimoto, Itaru; Sakaguchi, Takahisa; Gotoda,

Masaharu

PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan SOURCE: PCT Int. Appl., 95 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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PATENT NO. KIND DATE APPLICATION NO. DATE
      WO 2005063713 A1 20050714 WO 2004-JP19223 20041222
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EP 1698623 A1 20060906 EP 2004-807580 20041222
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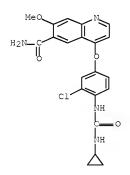
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XA 2006005226 A 20070425 ZA 2006-5226 20060622
KR 2006113759 A 20061102 KR 2006-713993 20060712
KR 804566 B1 20080220
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KR 2007107185 A 20071106 KR 2007-722490 20071001
KR 870681 B1 2008126
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RITY APPLN. INFO.:
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                                                        JP 2003-430939 A 20031225
CN 2004-80036184 A3 20041222
PRIORITY APPLN. INFO.:
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KR 2007-722490 A3 20071001
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AB
       sulfate, methanesulfonate, or ethanesulfonate of 4-[3-chloro-4-
       (cyclopropylamino-carbonyl)aminophenoxy]-7-methoxy-6- quinolinecarboxamide or
       crystals of a solvate of any of these. The crystals have improved
       physicochem. and pharmacokinetic properties, and suitable for use as
       neovascularization inhibitors for treatment of related diseases.
ΙT
      857890-33-6P 857890-39-2P
      RL: PEP (Physical, engineering or chemical process); PKT
      (Pharmacokinetics); PRP (Properties); PYP (Physical process); SPN
      (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
      PREP (Preparation); PROC (Process); USES (Uses)
          (crystal of salt of 4-[3-chloro-4-(cyclopropylaminocarbonyl)amino-
          phenoxy]-7-methoxy-6-quinolinecarboxamide or solvate thereof as
          neovascularization inhibitor, and preparation thereof)
      857890-33-6 HCAPLUS
RN
CN
      6-Quinolinecarboxamide, 4-[3-chloro-4-
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 $\label{eq:condition} \begin{tabular}{ll} [(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-, hydrobromide (1:1) \\ (CA INDEX NAME) \end{tabular}$

CMF C21 H19 C1 N4 O4

RN 857890-39-2 HCAPLUS
CN 6-Quinolinecarboxamide, 4-[3-chloro-4 [[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-, methanesulfonate
 (1:1) (CA INDEX NAME)

CM 1
CRN 417716-92-8



CM 2

CRN 75-75-2

CMF C H4 O3 S

857890-43-8P 857890-45-0P TТ RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses) (crystal of salt of 4-[3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy]-7-methoxy-6-quinolinecarboxamide or solvate thereof as neovascularization inhibitor, and preparation thereof) 857890-43-8 HCAPLUS RN CN 6-Quinolinecarboxamide, 4-[3-chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-, monomethanesulfonate, compd. with sulfonylbis[methane] (9CI) (CA INDEX NAME) CM1 CRN 417716-92-8 CMF C21 H19 C1 N4 O4

CM 2

CRN 75-75-2

CMF C H4 O3 S

CM 3

CRN 67-71-0 CMF C2 H6 O2 S

RN 857890-45-0 HCAPLUS
CN 6-Quinolinecarboxamide, 4-[3-chloro-4 [[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-, acetate
 methanesulfonate (1:?:?) (CA INDEX NAME)

CM 1

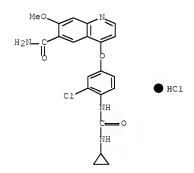
CRN 417716-92-8 CMF C21 H19 C1 N4 O4

CM 2

CRN 75-75-2 CMF C H4 O3 S

CM 3

CRN 64-19-7 CMF C2 H4 O2



RN 857890-35-8 HCAPLUS
CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-,
4-methylbenzenesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 417716-92-8 CMF C21 H19 C1 N4 O4

$$\begin{array}{c|c} \text{MeO} & \text{N} \\ \text{H}_2\text{N} & \text{C}_1 & \text{NH} \\ & \text{NH} & \text{NH} \end{array}$$

CM 2

CRN 104-15-4 CMF C7 H8 O3 S

RN 857890-37-0 HCAPLUS

6-Quinolinecarboxamide, 4-[3-chloro-4-

 $\label{eq:condition} \begin{tabular}{ll} [(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-, sulfate (1:1) (CAINDEX NAME) \end{tabular}$

CM 1

CN

CRN 417716-92-8 CMF C21 H19 C1 N4 O4

CM 2

CRN 7664-93-9

CMF H2 O4 S

CM 1

CRN 417716-92-8 CMF C21 H19 C1 N4 O4

CM 2

CRN 75-75-2 CMF C H4 O3 S

RN 857890-47-2 HCAPLUS CN Ethanesulfonic acid, compd. with 4-[3-chloro-4-

```
[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-6-
     quinolinecarboxamide (1:1) (CA INDEX NAME)
     CM
     CRN 417716-92-8
     CMF C21 H19 C1 N4 O4
 H2N-
     CM
          2
     CRN 594-45-6
     CMF C2 H6 O3 S
RN
     857890-49-4 HCAPLUS
CN
     Ethanesulfonic acid, compd. with 4-[3-chloro-4-
     [[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-6-
     quinolinecarboxamide and sulfonylbis[methane] (1:1:?) (9CI) (CA INDEX
     NAME)
     CM
     CRN 417716-92-8
     CMF C21 H19 C1 N4 O4
```

CM 2

CRN 594-45-6 CMF C2 H6 O3 S

CM 3

CRN 67-71-0 CMF C2 H6 O2 S

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2004:1016020 HCAPLUS Full-text

DOCUMENT NUMBER: 141:427993

TITLE: Polymorphous crystal of

4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-

7-methoxy-6-qunolinecarboxamide and method for

preparation thereof

INVENTOR(S): Arimoto, Itaru; Yoshizawa, Kazuhiro; Kamada, Atsushi

PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan SOURCE: PCT Int. Appl., 79 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

1	PATENT	NO.			KIND DATE			APPLICATION NO.							DATE		
	WO 2004101526			A1 20041125			WO 2004-JP5788										
	W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	KZ,	LC,
		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	NA,	ΝI,
		NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,
		TJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	zw
	RW:	BW,	GH,	GM,	KE,	LS,	MW,	ΜZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,
		BY,	KG,	KΖ,	MD,	RU,	ТJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,
		ES,	FI,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC,	NL,	PL,	PT,	RO,	SE,	SI,
		SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,
		TD,	ΤG														
1	US 20070117842					A1 20070524			US 2006-553927						20060630		
PRIOR	RIORITY APPLN. INFO.:									US 2	003-	4646	74P		P 2	0030	422
									1	WO 2	004-	JP57	88	1	₩ 2	0040	422

AB Disclosed are a polymorphous crystal (A) of 4-(3-chloro-4-(cyclopropylaminocarbonyl) aminophenoxy)-7-methoxy-6- qunolinecarboxamide (I) having a diffraction peak at a diffraction angle (20 ± 0.2°) of 15.75° in the powder X-ray diffractometry; and a polymorphous crystal (B) of I having a

diffraction peak at a diffraction angle (20 \pm 0.2°) of 21.75° in the powder X-ray diffractometry.

IT 417716-92-8P

CN

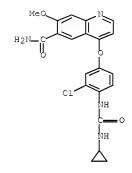
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-qunolinecarboxamide polymorphous crystals)

RN 417716-92-8 HCAPLUS

6-Quinolinecarboxamide, 4-[3-chloro-4-

[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:314913 HCAPLUS Full-text

DOCUMENT NUMBER: 136:340689

TITLE: Preparation of urea derivatives containing nitrogenous

aromatic ring compounds as inhibitors of angiogenesis INVENTOR(S): Funahashi, Yasuhiro; Tsuruoka, Akihiko; Matsukura,

Funahashi, Yasuhiro; Tsuruoka, Akihiko; Matsukura, Masayuki; Haneda, Toru; Fukuda, Yoshio; Kamata, Junichi; Takahashi, Keiko; Matsushima, Tomohiro; Miyazaki, Kazuki; Nomoto, Kenichi; Watanabe, Tatsuo; Obaishi, Hiroshi; Yamaguchi, Atsumi; Suzuki, Sachi; Nakamura, Katsuji; Mimura, Fusayo; Yamamoto, Yuji;

Matsui, Junji; Matsui, Kenji; Yoshiba, Takako; Suzuki,

Yasuyuki; Arimoto, Itaru Eisai Co., Ltd., Japan

PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan SOURCE: PCT Int. Appl., 699 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

```
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
                     GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
                     LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
                     PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
                     US, UZ, VN, YU, ZA, ZW
               RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
                     DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
                     BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
        BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, ID, IG

AL 2426461 A1 20020425 CA 2001-2426461 20011019

AU 2001095986 A 20020429 AU 2001-95986 20011019

HU 2003002603 A2 20031128 HU 2003-2603 20011019

CN 1478078 A 20040225 CN 2001-819710 20011019

CN 1308310 C 20070404

EP 1415987 A1 20040506 EP 2001-976786 20011019

EP 1415987 B1 20070228
               R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
                     IE, FI, CY, TR
        EP 1506962
                                                  20050216 EP 2004-25700
                                       A2
                                                                                                         20011019
                                       A3 20050302
B1 20080702
        EP 1506962
        EP 1506962
               R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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        TE, F1, C1, 1K

NZ 525324

A 20050324

NZ 2001-525324

JP 3712393

B2 20051102

JP 2002-536056

RU 2264389

C2 20051120

RU 2003-114740

AT 355275

T 20060315

AT 2001-976786

AU 2001295986

B2 20060817

AU 2001-295986

EP 1777218

B1 20081231

EP 1777218

B1 20081231
                                                                                                         20011019
                                                                                                        20011019
                                                                                                        20011019
                                                                                                        20011019
                                                                                                        20011019
                                                                                                        20011019
               R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC,
NL, PT, SE, TR
                                                                    NO 2007-4657 20070912
JP 2000-320420 A 20001020
JP 2000-386195 A 20001220
JP 2001-46685 A 20010222
AU 2001-295986 A3 20011019
AU 2001-95986 TO 20011019
CN 2001-819710 A3 20011019
EP 2001-976786 A3 20011019
JP 2002-536056 A3 20011019
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WO 2001-JP9221 W 20011019
US 2003-420466 A3 20030418 US 2005-293785 A1 20051202

OTHER SOURCE(S): GΙ

MARPAT 136:340689

AB N-aryl or N-heteroarylurea derivs, represented by the general formula Aq-Xq-Yg-Tg1 or salts thereof, or hydrates of both [wherein Ag = (un)substituted C6-14 aryl or 5- to 14-membered heterocyclic group; Xg = single bond, O, S, C1-6 alkylene, SO, SO2, (un)substituted NH; Yg = (un)substituted C6-14 aryl, 5- to 14-membered heterocyclic group, C1-8 alkyl, C3-8 alicyclic hydrocarbyl, C6-14 aryl-C1-6 alkyl, 5- to 14-membered heteroaryl-C1-6 alkyl, (CH2)gSO2 (g = 1-8), (CH2) faCH:CH(CH2) fb (fa, fb = 0, 1, 2, 3), etc.; and <math>Tq1 = a group of the general formula -Eg-CO-NRg1(Zg) or Q; wherein Eg = a single bond, (un) substituted NH; Rg1 = H, (un) substituted C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C3-8 aliphatic hydrocarbyl, etc.; Zg = C1-8 alkyl, C3-8 alicyclic hydrocarbyl, C6-14 aryl, etc.; Zg1, Zg2 = (a) a single bond, (b) C1-6 alkylene optionally having ≥1 atoms selected from O, S, and N in the middle or the terminus of the chain and optionally substituted with oxo, (c) (un)substituted C2-6 alkenyl] are prepared These compds. are also inhibitors of vascular endothelial growth factor receptor kinase (VEGFR2 kinase) and are useful as antitumor agents against hemangioma, pancreatic cancer, stomach cancer, colon cancer, breast cancer, prostate cancer, lung cancer, brain tumor, leukemia, or ovarian cancer, as cancer metastasis inhibitors, and for the treatment of retina neovascularization, diabetic retinopathy, atherosclerosis, or inflammatory diseases such as osteoarthritis, rheumatoid arthritis, psoriasis, or delayed hypersensitivity. Thus, to solution of 334 mg 4-[6-(4benzyloxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenylamine in 4 mL DMF were added 0.066 mL pyridine and 0.102 mL Ph chlorocarbonate and stirred at room temperature for 2.5 h to give 330 mg N-[4-[6-(4-benzyloxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7Hpyrrolo[2,3-d]pyrimidin-4-yloxy]-2- chlorophenyl]-N'-cyclopropylurea which (260 mg) was hydrogenolyzed over platinum oxide in ethanol overnight to give 160 mg N-[4-[6-(4-hydroxyphenyl)-7-(2-trimethylsilylethoxymethyl)-7Hpyrrolo[2,3-d]pyrimidin-4-yloxy]-2-chlorophenyl]-N'-cyclopropylurea (I). I showed IC50 of 0.02 nM for inhibiting the vascular endothelial growth factor (VEGF)-stimulated sandwich tube formation in vascular endothelial cell.

417716-92-8P 417719-50-7P TT

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of urea derivs. containing nitrogenous aromatic ring compds.

as

CN

angiogenesis inhibitors for prevention or treatment of diseases) 417716-92-8 HCAPLUS

RN

6-Ouinolinecarboxamide, 4-[3-chloro-4-

[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy- (CA INDEX NAME)

RN 417719-50-7 HCAPLUS
CN 6-Quinolinecarboxamide, 4-[3-chloro-4-[[[[(1R,2S)-2-fluorocyclopropyl]amino]carbonyl]amino]phenoxy]-7-methoxy-, rel- (CA INDEX NAME)

Relative stereochemistry.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> => d stat que 123 L1 STR

NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES: RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 30

STEREO ATTRIBUTES: NONE

L3 107 SEA FILE=REGISTRY SSS FUL L1 L4 STR

NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 30

STEREO ATTRIBUTES: NONE

L5 14 SEA FILE=REGISTRY SUB=L3 SSS FUL L4 L6 26 SEA FILE=HCAPLUS ABB=ON PLU=ON L5

L7 20506 SEA FILE=HCAPLUS ABB=ON PLU=ON ("SMALL-CELL LUNG CARCINOMA"/C
V OR "CARCINOMA (L) PULMONARY SMALL-CELL"/CV OR "LUNG (L)
SMALL-CELL CARCINOMA"/CV OR "LUNG, NEOPLASM (L) SMALL-CELL
CARCINOMA"/CV OR "LUNG OAT CELL CARCINOMA"/CV OR "LUNG SMALL
CELL CANCER"/CV) OR ("SMALL CELL CARCINOMA"/CV OR "SMALL CELL

LUNG CANCER"/CV OR "SMALL LUNG CELL CARCINOMA"/CV OR "SMALL-CEL

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L CARCINOMA (LUNG) "/CV OR "SMALL-CELL CARCINOMA (PULMONARY) "/CV
               ) OR SMALL(L)CELL(L)LUNG(L)(CANCER? OR CARCINOMA)
L8
              4 SEA FILE=HCAPLUS ABB=ON PLU=ON L6 AND L7
L9
             22 SEA FILE=HCAPLUS ABB=ON PLU=ON L6 NOT L8
             18 SEA FILE=HCAPLUS ABB=ON PLU=ON L9 AND (?CANCER? OR ?CARCIN?
L10
               OR ?TUMOR? OR ?MALIG? OR ?NEOPLAS?)
L11
              6 SEA FILE=HCAPLUS ABB=ON PLU=ON L10 AND (LUNG OR PULMON?)
L12
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L13
           2815 SEA FILE=HCAPLUS ABB=ON PLU=ON "WATANABE T"/AU OR WATANABE T
                ?/AU OR ("WATANABE TATSUO"/AU OR "WATANABE TATSURO"/AU)
            949 SEA FILE=HCAPLUS ABB=ON PLU=ON "OKADA M"/AU OR OKADA M ?/AU
L14
               OR "OKADA MASAYUKI"/AU
L15
             41 SEA FILE=HCAPLUS ABB=ON PLU=ON "TSURUOKA A"/AU OR "TSURUOKA
               AKIHIKO"/AU
L16
            19 SEA FILE=HCAPLUS ABB=ON PLU=ON L12 AND (L13 OR L14 OR L15)
             8 SEA FILE=HCAPLUS ABB=ON PLU=ON L13 AND (L14 OR L15)
L17
L18
             1 SEA FILE=HCAPLUS ABB=ON PLU=ON L14 AND L15
            93 SEA FILE=REGISTRY ABB=ON PLU=ON L3 NOT L5
L19
L20
            16 SEA FILE=HCAPLUS ABB=ON PLU=ON L19
L22
            14 SEA FILE=HCAPLUS ABB=ON PLU=ON (L12 OR L13 OR L14 OR L15)
               AND (L6 OR L20)
L23
             23 SEA FILE=HCAPLUS ABB=ON PLU=ON ((L16 OR L17 OR L18) OR L22)
               NOT (L8 OR L11)
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=> d ibib abs hitstr 123 1-23

LANGUAGE:

L23 ANSWER 1 OF 23 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2009:464003 HCAPLUS Full-text

In-situ characterization of transport properties of TITLE:

superconducting (Cu, C)-1201 films

AUTHOR(S): Kikunaga, K.; Yamamoto, Y.; Mitsunaga, M.; Mahara,

Y.; Tanaka, Y.; Kikuchi, N.; Tokiwa, K.; Watanabe,

T.; Terada, N.

CORPORATE SOURCE: Department of Nano Structures and Advanced Materials,

Kagoshima University, 1-21-40 Korimoto, Kagoshima,

890-0065, Japan

SOURCE: Journal of Physics: Conference Series (2009), 150, No

pp. given

CODEN: JPCSDZ; ISSN: 1742-6588

URL: http://www.iop.org/EJ/article/1742-

6596/150/5/052108/jpconf9_150_052108.pdf

PUBLISHER: Institute of Physics Publishing DOCUMENT TYPE: Journal; (online computer file) English

Transport properties of (Cu, C)-1201 thin films have been characterized by insitu four probe method without breaking vacuum, subsequent to their growth by pulsed laser deposition, in order to clarify intrinsic transport properties. Owing to the in-situ measurements, degradation of contact resistance and normal state conductivity were successfully suppressed. Obtained results reveal the pos. correlation between Tc and normal state conductivity σ at 290 K, and that between Tc and temperature coefficient of resistivity (TCR) at 290 K. The films exhibit $Tc(\rho = 0) > 20$ K on the cases of $\sigma[290 \text{ K}] > 4 \times 102 \text{ S/cm}$ and TCR > 1.5×10^{-3} K-1. The high Tc with low conductivity of (Cu, C)-1201 films indicates the presence of extrinsic defects such as grain boundaries. The absence of saturation of Tc with an increase of TCR indicates doping level

of the (Cu, C)-1201 films in this study should be in between under-doped to optimally-doped states. They suggest there would be some room for further increases of Tc.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 2 OF 23 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2008:945676 HCAPLUS Full-text

DOCUMENT NUMBER: 150:70494

TITLE: Anti-tumor effect of E7080, a novel angiogenesis

inhibitor

AUTHOR(S): Koyama, Noriyuki; Magario, Naoki; Yamamoto, Yuji;

Matsui, Junji; Tsuruoka, Akihiko

CORPORATE SOURCE: Clin. Res. Cent., Eisai Co., Ltd., Tokyo, 112-8088,

Japan

SOURCE: Nippon Yakurigaku Zasshi (2008), 132(2), 100-104

CODEN: NYKZAU; ISSN: 0015-5691

PUBLISHER: Nippon Yakuri Gakkai DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese

AB A review on the inhibitory activity against angiogenesis and VEGF receptor kinase selectivity mechanism of E7080. Antitumor efficacies in preclin. study of E7080, mono- or combination with other neoplasm inhibitors are also discussed.

IT 417716-92-8

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(E 7080; anti-tumor effect of E7080, novel angiogenesis inhibitor)

RN 417716-92-8 HCAPLUS

CN 6-Ouinolinecarboxamide, 4-[3-chloro-4-

[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy- (CA INDEX NAME)

INVENTOR(S):

L23 ANSWER 3 OF 23 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2008:940616 HCAPLUS Full-text

DOCUMENT NUMBER: 149:239320

TITLE: Composition for treatment of undifferentiated-type of

gastric cancer Yamamoto, Yuji

PATENT ASSIGNEE(S): Eisai R & D Management Co., Ltd., Japan

SOURCE: PCT Int. Appl., 221pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

RN

CN

417716-92-8 HCAPLUS

6-Quinolinecarboxamide, 4-[3-chloro-4-

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PATENT NO.
                   KIND DATE APPLICATION NO.
                                                               DATE
                                         ______
     _____
                      ----
                       A1 20080807 WO 2008-JP51697 20080128
    WO 2008093855
        W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ,
            CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES,
            FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE,
            KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD,
            ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH,
            PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM,
            TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
        RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,
            IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK,
            TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
            TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
            AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:
                                          US 2007-887006P P 20070129
OTHER SOURCE(S):
                       MARPAT 149:239320
     Disclosed are: a therapeutic agent, a kit and a treatment method for
AB
     undifferentiated-type of gastric cancer; and a pharmaceutical composition, a
     kit and a treatment method which are more effective on a living body having at
     least one cell selected from the group consisting of a cell over-expressing
     FGFR2 and a cell expressing a FGFR2 mutant. A combination of a FGFR2
     inhibitor and a therapeutic substance for gastric cancer is more effective on
     undifferentiated-type of gastric cancer. The combination of a FGFR2 inhibitor
     and a therapeutic substance for gastric cancer is more effective on a living
     body having at least one cell selected from the group consisting of a cell
     over-expressing FGFR2 and a cell expressing a FGFR2 mutant. For example, the
     synergistic effect of combination of 4-(3-chloro-4-
     [cyclopropylaminocarbonyl)aminophenoxy]-7- methoxy-6-quinolinecarboxamide and
     irinotecan hydrochloride in HSC-30 human gastric carcinoma cell-bearing mice
     was examined
     417716-92-8, 4-(3-Chloro-4-[cyclopropylaminocarbonyl)aminophenoxy]-
     7-methoxy-6-quinolinecarboxamide 417717-44-3,
    N6-Methoxy-4-(3-chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-
     methoxy-6-quinolinecarboxamide 857890-39-2
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (composition for treatment of undifferentiated-type of gastric cancer
containing
       quinoline derivs. in combination with antitumor agent or FGFR2
       inhibitor)
```

[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy- (CA INDEX NAME)

RN 417717-44-3 HCAPLUS
CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-N,7-dimethoxy- (CA INDEX NAME)

```
RN 857890-39-2 HCAPLUS
CN 6-Quinolinecarboxamide, 4-[3-chloro-4-
[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-, methanesulfonate
(1:1) (CA INDEX NAME)

CM 1

CRN 417716-92-8
CMF C21 H19 C1 N4 O4
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CM 2

CRN 75-75-2 CMF C H4 O3 S

22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 4 OF 23 HCAPLUS COPYRIGHT 2009 ACS on STN 2008:890824 HCAPLUS Full-text ACCESSION NUMBER:

DOCUMENT NUMBER:

149:167954 TITLE: Composition for treatment of pancreatic cancer

INVENTOR(S):

Yamamoto, Yuji PATENT ASSIGNEE(S): Eisai R & D Management Co., Ltd., Japan

SOURCE: PCT Int. Appl., 126pp.

CODEN: PIXXD2

DOCUMENT TYPE: LANGUAGE:

Patent Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA:	PATENT NO.				KIN	D	DATE			APPL	ICAT	DATE						
						-												
WO	WO 2008088088				A1 20080724			1	WO 2	008-		20080118						
	W:	ΑE,	AG,	AL,	AM,	AO,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BH,	BR,	BW,	BY,	BZ,	
		CA,	CH,	CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DO,	DZ,	EC,	EE,	EG,	ES,	
		FI,	GB,	GD,	GE,	GH,	GM,	GT,	HN,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	
		KG,	KM,	KN,	KP,	KR,	KΖ,	LA,	LC,	LK,	LR,	LS,	LT,	LU,	LY,	MA,	MD,	
		ME,	MG,	MK,	MN,	MW,	MX,	MY,	MZ,	NA,	NG,	NΙ,	NO,	NZ,	OM,	PG,	PH,	
		PL,	PT,	RO,	RS,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SM,	SV,	SY,	ΤJ,	TM,	
		TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	ZA,	ZM,	ZW				
	RW:	AT.	BE.	BG.	CH.	CY.	CZ.	DE.	DK.	EE.	ES.	FI.	FR.	GB.	GR.	HR.	HU.	

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IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK,
             TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
             TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
             AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO .:
                                            US 2007-885733P
                                                              P 20070119
                                            US 2007-887010P
                                                               P 20070129
OTHER SOURCE(S):
                         MARPAT 149:167954
AB
     Disclosed are a pharmaceutical composition having excellent antitumor
     activity, and a method for treating a cancer. Specifically, excellent
     antitumor activity is achieved when 4-(3-chloro-4-
     (cyclopropylaminocarbonyl)aminophenoxy)-7- methoxy-6-quinolinecarboxamide (A)
     or an analogous compound thereof, a pharmacol. acceptable salt thereof or a
     solvate of any of them is used in combination with gemcitabine or erlotinib, a
     pharmacol. acceptable salt thereof or a solvate of any of them. For example,
     the effect of combination of a compound A 3 mg/kg and gemcitabine
     hydrochloride 200 mg/kg on AsPC-1 human pancreatic cancer cell-bearing mice
     was examined
     417716-92-8, 4-(3-Chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-
     7-methoxy-6-quinolinecarboxamide 417717-05-6,
     4-(3-Chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-methoxyethoxy)-
     6-quinolinecarboxamide 417717-07-8,
     4-(3-Chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-(4-
     morpholino)ethoxy)-6-quinolinecarboxamide 417717-10-3,
     4-(3-Chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-hydroxyethoxy)-
     6-quinolinecarboxamide 417717-15-8,
     4-(3-Chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-((2S)-2,3-
     dihydroxypropyl)oxy-6-quinolinecarboxamide 417717-22-7,
     N6-Cyclopropyl-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-
     methoxy-6-quinolinecarboxamide 417717-23-8,
     N6-(2-Methoxyethyl)-4-(3-chloro-4-
     (((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-
     quinolinecarboxamide 417717-35-2,
     N6-(2-Hydroxyethyl)-4-(3-chloro-4-
     (((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-
     quinolinecarboxamide 417717-41-0,
     N6-(2-Fluoroethyl)-4-(3-chloro-4-
     (((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-
     quinolinecarboxamide 417717-44-3,
     N6-Methoxy-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-
     methoxy-6-quinolinecarboxamide 417717-76-1,
     N6-Methyl-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-
     methoxy-6-quinolinecarboxamide 417717-77-2,
     N6-Ethyl-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-
     methoxy-6-quinolinecarboxamide 417718-41-3,
     N-(2-Fluoro-4-((6-carbamoyl-7-methoxy-4-[quinolyl)oxy)phenyl)-N'-
     cyclopropylurea 417719-21-2,
     4-(3-Fluoro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-methoxyethoxy)-
     6-quinolinecarboxamide 417719-50-7,
     4-(3-Chloro-4-(cis-2-fluoro-cyclopropylaminocarbonyl)aminophenoxy)-7-
     methoxy-6-quinolinecarboxamide 417719-56-3,
     4-(3-Chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-ethoxyethoxy)-6-
     guinolinecarboxamide 417719-77-8,
     4-(3-Chloro-4-[(((cyclopropylamino)carbonyl)amino)phenoxy)-7-((2R)-2-
     hydroxy-3-(1-pyrrolidino)propoxy)-6-quinolinecarboxamide
     417719-84-7, N-(4-(6-(2-Cyanoethyl)carbamoyl-7-methoxy-4-
     quinoly1)oxy-2-fluoropheny1)-N'-cyclopropylurea 417720-85-5,
     N6-Methyl-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-(2-
     methoxyethoxy)-6-quinolinecarboxamide 857890-39-2
```

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical compns. containing urea derivs. in combination with gemcitabine or erlotinib)
RN 417716-92-8 HCAPLUS
CN 6-Quinolinecarboxamide, 4-[3-chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy- (CA INDEX NAME)

RN 417717-05-6 HCAPLUS
CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-(2-methoxyethoxy)- (CA
INDEX NAME)

RN 417717-07-8 HCAPLUS
CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-[2-(4-morpholinyl)ethoxy](CA INDEX NAME)

RN 417717-10-3 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4 [[(cyclopropylamino)carbonyl]amino]phenoxy]-7-(2-hydroxyethoxy)- (CA
 INDEX NAME)

RN 417717-15-8 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-[(2S)-2,3-dihydroxypropoxy]-(CA INDEX NAME)

Absolute stereochemistry.

RN 417717-22-7 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-N-cyclopropyl-7-methoxy- (CA INDEX NAME)

RN 417717-23-8 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-N-(2-methoxyethyl)(CA INDEX NAME)

RN 417717-35-2 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-N-(2-hydroxyethyl)-7-methoxy(CA INDEX NAME)

RN 417717-41-0 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

 $\label{lem:condition} \begin{tabular}{ll} $[(cyclopropylamino)carbonyl]=N-(2-fluoroethyl)-7-methoxy-(CA INDEX NAME) \end{tabular}$

RN 417717-44-3 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

[[(cyclopropylamino)carbonyl]amino]phenoxy]-N,7-dimethoxy- (CA INDEX NAME)

RN 417717-76-1 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

RN 417717-77-2 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

[[(cyclopropylamino)carbonyl]amino]phenoxy]-N-ethyl-7-methoxy- (CA INDEX NAME)

RN 417718-41-3 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[4-[[(cyclopropylamino)carbonyl]amino]-3-fluorophenoxy]-7-methoxy- (CA INDEX NAME)

RN 417719-21-2 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[4-[[(cyclopropylamino)carbonyl]amino]-3-fluorophenoxy]-7-(2-methoxyethoxy)- (CA INDEX NAME)

RN 417719-50-7 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-[[[[(1R,2S)-2-fluorocyclopropyl]amino]carbonyl]amino]phenoxy]-7-methoxy-, rel- (CA INDEX NAME)

Relative stereochemistry.

$$\begin{array}{c} \text{MeO} \\ \text{H2N} \\ \end{array}$$

RN 417719-56-3 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-(2-ethoxyethoxy)- (CA INDEX NAME)

RN 417719-77-8 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-[(2R)-2-hydroxy-3-(1pyrrolidinyl)propoxy]- (CA INDEX NAME)

Absolute stereochemistry.

RN 417719-84-7 HCAPLUS

CN 6-Quinolinecarboxamide, N-(2-cyanoethyl)-4-[4[[(cyclopropylamino)carbonyl]amino]-3-fluorophenoxy]-7-methoxy- (CA INDEX NAME)

RN 417720-85-5 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-(2-methoxyethoxy)-N-methyl(CA INDEX NAME)

RN 857890-39-2 HCAPLUS
CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-, methanesulfonate
(1:1) (CA INDEX NAME)

CM 1

CRN 417716-92-8 CMF C21 H19 C1 N4 O4

CM 2

CRN 75-75-2 CMF C H4 O3 S

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 5 OF 23 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2008:281590 HCAPLUS Full-text

DOCUMENT NUMBER: 148:323091

TITLE: Antitumor agent for undifferentiated gastric cancer INVENTOR(S): Yamamoto, Yuji; Matsushima, Tomohiro; Tsurwoka, Akihiko; Obaishi, Hiroshi; Nakagawa, Takayuki

PATENT ASSIGNEE(S): Eisai R & D Management Co., Ltd., Japan

SOURCE: PCT Int. Appl., 138pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

GΙ

PA	TENT	NO.			KIND		DATE		APPLICATION NO.									
WO	2008		A1		20080306							20070827						
	W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BH,	BR,	BW,	BY,	BZ,	CA,	
		CH,	CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DO,	DZ,	EC,	EE,	EG,	ES,	FI,	
		GB,	GD,	GE,	GH,	GM,	GT,	HN,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	
		KΜ,	KN,	KP,	KR,	KΖ,	LA,	LC,	LK,	LR,	LS,	LT,	LU,	LY,	MA,	MD,	ΜE,	
		MG,	MK,	MN,	MW,	MX,	MY,	MZ,	NA,	NG,	ΝI,	NO,	NΖ,	OM,	PG,	PH,	PL,	
		PT,	RO,	RS,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SM,	SV,	SY,	ТJ,	TM,	TN,	
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		IS,	ΙT,	LT,	LU,	LV,	MC,	MT,	NL,	PL,	PT,	RO,	SE,	SI,	SK,	TR,	BF,	
		ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG,	B₩,	
		GH,	GM,	KE,	LS,	MW,	ΜZ,	NΑ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	
		BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM										
EP	EP 2065372						A1 20090603				007-	8065		20070827				
	R:	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	HU,	ΙE,	
		IS,	ΙT,	LI,	LT,	LU,	LV,	MC,	MT,	NL,	PL,	PT,	RO,	SE,	SI,	SK,	TR,	
		AL,	ΒA,	HR,	MK,	RS												
KR	2009	0435	78		A		2009	0506		KR 2009-705657					20090319			
PRIORIT	RIORITY APPLN. INFO.:										JP 2006-230816					A 20060828		
										WO 2	007-	JP67	880		W 2	0070	827	
OTHER S	OURCE	(S):			MARPAT 148:323091													

AB A compound represented by the general formula (I), a pharmacol. acceptable salt thereof, or a solvate of the compound or the salt can exert its effect more effectively on undifferentiated gastric cancer, and can also exerts its effect more effectively on a living body having at least one member selected from the group consisting of a cell over-expressing FGFR2 and a cell expressing mutant FGFR2.

Ι

- IT 417716-92-8P, 4-(3-Chloro-4 (cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)
 - (quinolinylurea analogs as antitumor agents for undifferentiated gastric cancer)
- RN 417716-92-8 HCAPLUS
- CN 6-Quinolinecarboxamide, 4-[3-chloro-4-
 - [[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy- (CA INDEX NAME)

```
ΤТ
     417717-05-6, 4-(3-Chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-
     7-(2-methoxyethoxy)-6-quinolinecarboxamide 417717-07-8
     417717-10-3 417717-15-8,
     4-(3-Chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-((2S)-2,3-
     dihydroxypropyl)oxy-6-quinolinecarboxamide 417717-22-7
     417717-23-8 417717-35-2 417717-41-0
     417717-44-3, N6-Methoxy-4-(3-chloro-4-
     (((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-
     quinolinecarboxamide 417717-76-1 417717-77-2
     417718-41-3 417719-21-2 417719-50-7
     417719-56-3 417719-77-8 417719-84-7
     417720-85-5
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (quinolinylurea analogs as antitumor agents for undifferentiated
        gastric cancer)
RN
     417717-05-6 HCAPLUS
CN
     6-Quinolinecarboxamide, 4-[3-chloro-4-
     [[(cyclopropylamino)carbonyl]amino]phenoxy]-7-(2-methoxyethoxy)- (CA
     INDEX NAME)
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RN 417717-07-8 HCAPLUS
CN 6-Quinolinecarboxamide, 4-[3-chloro-4-
[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-[2-(4-morpholinyl)ethoxy]-
```

(CA INDEX NAME)

RN 417717-10-3 HCAPLUS
CN 6-Quinolinecarboxamide, 4-[3-chloro-4 [[(cyclopropylamino)carbonyl]amino]phenoxy]-7-(2-hydroxyethoxy)- (CA INDEX NAME)

RN 417717-15-8 HCAPLUS
CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-[(2S)-2,3-dihydroxypropoxy](CA INDEX NAME)

Absolute stereochemistry.

$$\begin{array}{c} \text{OH} \\ \text{H}_{2}\text{N} \\ \end{array}$$

RN 417717-22-7 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4 [[(cyclopropylamino)carbonyl]amino]phenoxy]-N-cyclopropyl-7-methoxy- (CA INDEX NAME)

RN 417717-23-8 HCAPLUS
CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

 $\label{locality} \begin{tabular}{ll} [(\mbox{oyclopropylamino})\mbox{carbonyl}] \mbox{amino}] phenoxy] -7-methoxy-N-(2-methoxyethyl)-(CA INDEX NAME) \end{tabular}$

RN 417717-35-2 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

[[(cyclopropylamino)carbonyl]amino]phenoxy]-N-(2-hydroxyethyl)-7-methoxy-(CA INDEX NAME)

RN 417717-41-0 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

[[(cyclopropylamino)carbonyl]amino]phenoxy]-N-(2-fluoroethyl)-7-methoxy-(CA INDEX NAME)

RN 417717-44-3 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

 $\label{eq:condition} \begin{tabular}{ll} $[(cyclopropylamino)carbonyl]$-M, 7-dimethoxy- & (CA INDEX NAME) \end{tabular}$

RN 417717-76-1 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

RN 417717-77-2 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

RN 417718-41-3 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[4-[[(cyclopropylamino)carbonyl]amino]-3-fluorophenoxy]-7-methoxy- (CA INDEX NAME)

RN 417719-21-2 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[4-[[(cyclopropylamino)carbonyl]amino]-3-fluorophenoxy]-7-(2-methoxyethoxy)- (CA INDEX NAME)

RN 417719-50-7 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-[[[[(1R,2S)-2-fluorocyclopropyl]amino]carbonyl]amino]phenoxy]-7-methoxy-, rel- (CA INDEX NAME)

Relative stereochemistry.

RN 417719-56-3 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-(2-ethoxyethoxy)- (CA INDEX NAME)

RN 417719-77-8 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-[(2R)-2-hydroxy-3-(1-pyrrolidinyl)propoxy]- (CA INDEX NAME)

Absolute stereochemistry.

RN 417719-84-7 HCAPLUS

CN 6-Quinolinecarboxamide, N-(2-cyanoethyl)-4-[4-[[(cyclopropylamino)carbonyl]amino]-3-fluorophenoxy]-7-methoxy- (CA INDEX NAME)

RN 417720-85-5 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-(2-methoxyethoxy)-N-methyl(CA INDEX NAME)

19 REFERENCE COUNT: THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT L23 ANSWER 6 OF 23 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2007:509696 HCAPLUS Full-text DOCUMENT NUMBER: 146:455231 TITLE: Use of combination of anti-angiogenic substance and c-kit kinase inhibitor Yamamoto, Yuji INVENTOR(S): PATENT ASSIGNEE(S): Eisai R & D Management Co., Ltd., Japan PCT Int. Appl., 102pp. SOURCE: CODEN: PIXXD2 DOCUMENT TYPE: Patent LANGUAGE: Japanese FAMILY ACC. NUM. COUNT: 2 PATENT INFORMATION: PATENT NO. KIND DATE APPLICATION NO. DATE ----_____ 20061107 WO 2007052850 A1 20070510 WO 2006-JP322516 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM EP 1949902 A1 20080730 EP 2006-832529 20061107 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS PRIORITY APPLN. INFO.: JP 2005-322946 A 20051107 WO 2006-JP322516 W 20061107 OTHER SOURCE(S): MARPAT 146:455231 AB Disclosed are a pharmaceutical composition having an excellent anti-tumor effect, and a therapeutic method for cancer. 4-(3-Chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7 -methoxy-6-quinolinecarboxamide or an analog thereof can be used in combination with a substance having a c-kit kinase-inhibiting activity to produce an excellent anti-tumor effect. For example, the effect of combination of 4-(3-Chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7 -methoxy-6-quinolinecarboxamide methanesulfonate and imatinib on human gastrointestinal stromal tumor cell (GIST882 cell)-bearing model mice was examined 417716-92-8, 4-[3-Chlcoro-4-ΤТ (cyclopropylaminocarbonyl)aminophenoxy]-7-methoxy-6-quinolinecarboxamide 417717-05-6, 4-[3-Chlcoro-4-(cyclopropylaminocarbonyl)aminophenoxy]-7-(2-methoxyethoxy)-6quinolinecarboxamide 417717-07-8, 4-[3-Chloro-4-(cyclopropylaminocarbonyl)aminophenoxy]-7-[2-(4morpholino) ethoxy-6-quinolinecarboxamide 417717-10-3, 4-(3-Chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-(2hydroxyethoxy)-6-quinolinecarboxamide 417717-15-8,

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4-(3-Chloro-4-[(cyclopropylamino)carbonyl]amino]phenoxy]-7-[(2S)-2,3-
dihydroxypropyl)oxy-6-quinolinecarboxamide 417717-22-7,
N6-Cyclopropyl-4-(3-chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-
methoxy-6-quinolinecarboxamide 417717-23-8,
N6-(2-Methoxyethyl)-4-(3-chloro-4-
[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-6-
quinolinecarboxamide 417717-35-2,
N6-(2-Hydroxyethyl)-4-(3-chloro-4-
[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-6-
quinolinecarboxamide 417717-41-0,
N6-(2-Fluoroethyl)-4-(3-chloro-4-
[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-6-
quinolinecarboxamide 417717-44-3,
N6-Methoxy-4-(3-chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-
methoxy-6-quinolinecarboxamide 417717-76-1,
N6-Methyl-4-(3-chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-
methoxy-6-quinolinecarboxamide $17717-77-2,
N6-Ethyl-4-(3-chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-
methoxy-6-quinolinecarboxamide 417718-41-3,
N-[2-Fluoro-4-[(6-carbamoyl-7-methoxy-4-quinolyl)oxy]phenyl]-N'-
cyclopropylurea 417719-21-2,
4-(3-Fluoro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-(2-
methoxyethoxy)-6-quinolinecarboxamide 417719-50-7,
4-[3-Chloro-4-(cis-2-fluoro-cyclopropylaminocarbonyl)aminophenoxyl-7-
methoxy-6-quinolinecarboxamide 417719-56-3,
4-(3-Chloro-4-(cyclopropylaminocarbonyl) aminophenoxy) -7-(2-ethoxyethoxy) 6-
quinolinecarboxamide 417719-77-8,
4-[3-Chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-[(2R)-2-
hydroxy-3-(1-pyrrolidino)propoxy]-6-quinolinecarboxamide
417719-84-7, N-[4-[6-(2-Cyanoethyl)carbamoyl-7-methoxy-4-
quinolyl]oxy]-2-fluorophenyl]-N'-cyclopropylurea 417720-85-5,
N6-Methyl-4-(3-chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-(2-
methoxyethoxy)-6-quinolinecarboxamide 857890-39-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
   (use of combination of anti-angiogenic substance and c-kit kinase
   inhibitor)
417716-92-8 HCAPLUS
6-Quinolinecarboxamide, 4-[3-chloro-4-
[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy- (CA INDEX NAME)
```

RN

CN

RN 417717-05-6 HCAPLUS

CN

6-Quinolinecarboxamide, 4-[3-chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-(2-methoxyethoxy)- (CA INDEX NAME)

RN 417717-07-8 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4 [[(cyclopropylamino)carbonyl]amino]phenoxy]-7-[2-(4-morpholinyl)ethoxy] (CA INDEX NAME)

RN 417717-10-3 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-(2-hydroxyethoxy)- (CA INDEX NAME)

RN 417717-15-8 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-[(2S)-2,3-dihydroxypropoxy]-(CA INDEX NAME)

Absolute stereochemistry.

RN 417717-22-7 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

 $\label{local_condition} $$ [(\mbox{cylopropyl-7-methoxy-} \mbox{CA INDEX NAME})$$

RN 417717-23-8 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-N-(2-methoxyethyl)(CA INDEX NAME)

RN 417717-35-2 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

 $\begin{tabular}{ll} [(cyclopropylamino)carbonyl]amino] phenoxy]-N-(2-hydroxyethyl)-7-methoxy-(CA INDEX NAME) \end{tabular}$

RN 417717-41-0 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

 $\label{lem:condition} \begin{tabular}{ll} $[(cyclopropylamino)carbonyl]=N-(2-fluoroethyl)-7-methoxy-(CA INDEX NAME) \end{tabular}$

RN 417717-44-3 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

[[(cyclopropylamino)carbonyl]amino]phenoxy]-N,7-dimethoxy- (CA INDEX NAME)

RN 417717-76-1 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

 $\label{eq:condition} \begin{tabular}{ll} $[(cyclopropylamino)carbonyl]=mino]phenoxy]-7-methoxy-N-methyl- & (CA INDEX NAME) \\ \end{tabular}$

RN 417717-77-2 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

[[(cyclopropylamino)carbonyl]amino]phenoxy]-N-ethyl-7-methoxy- (CA INDEX NAME)

RN 417718-41-3 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[4-[[(cyclopropylamino)carbonyl]amino]-3-fluorophenoxy]-7-methoxy- (CA INDEX NAME)

RN 417719-21-2 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[4-[[(cyclopropylamino)carbonyl]amino]-3-fluorophenoxy]-7-(2-methoxyethoxy)- (CA INDEX NAME)

RN 417719-50-7 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-[[[[(1R,2S)-2fluorocyclopropyl]amino]carbonyl]amino]phenoxy]-7-methoxy-, rel- (CA INDEX NAME)

Relative stereochemistry.

RN 417719-56-3 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-(2-ethoxyethoxy)- (CA INDEX NAME)

EtO-CH2-CH2-ON
H2N-C
ONH
H2N-C
NH

RN 417719-77-8 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-[(2R)-2-hydroxy-3-(1pyrrolidinyl)propoxy]- (CA INDEX NAME)

Absolute stereochemistry.

RN 417719-84-7 HCAPLUS

RN 417720-85-5 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-(2-methoxyethoxy)-N-methyl-(CA INDEX NAME)

RN 857890-39-2 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 417716-92-8

CM :

CRN 75-75-2 CMF C H4 O3 S

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 7 OF 23 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2007:509694 HCAPLUS Full-text

DOCUMENT NUMBER: 146:455230

TITLE: Use of combination of anti-angiogenic substance and

c-kit kinase inhibitor

INVENTOR(S): Yamamoto, Yuji

PATENT ASSIGNEE(S): Eisai R & D Management Co., Ltd., Japan

SOURCE: PCT Int. Appl., 103pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PAT	TENT	NO.			KIN	D	DATE			APPL	ICAT	ION :	.00		D	ATE		
						_												
WO	WO 2007052849					A1 20070510					006-	20061107						
	W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,	
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,	
		GE,	GH,	GM,	GT,	HN,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KM,	KN,	
		KΡ,	KR,	KΖ,	LA,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	LY,	MA,	MD,	MG,	MK,	
		MN,	MW,	MX,	MY,	MZ,	NA,	NG,	NΙ,	NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	
		RS,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SM,	SV,	SY,	ТJ,	TM,	TN,	TR,	TT,	
		TZ,	UA,	UG,	US,	UZ,	VC,	VN,	ZA,	ZM,	zw							

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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
                                           AU 2006-309551
                                20070510
     AU 2006309551
                         Α1
                                                                   20061107
     CA 2627598
                         A1
                                20070510
                                            CA 2006-2627598
                                                                   20061107
     US 20090053236
                         A1
                                20090226
                                           US 2008-92539
                                                                   20080502
     CN 101316590
                        A
                               20081203
                                           CN 2006-80041355
                                                                   20080506
                                20080714
                                          KR 2008-713685
     KR 2008065698
                        Α
                                                                   20080605
PRIORITY APPLN. INFO .:
                                            JP 2005-322946 A 20051107
                                            WO 2006-JP322514 W 20061107
                        MARPAT 146:455230
OTHER SOURCE(S):
AB
     Disclosed are a pharmaceutical composition having an excellent anti-tumor
     effect, and a therapeutic method for cancer. 4-(3-Chloro-4-
     (cyclopropylaminocarbonyl)aminophenoxy)-7 -methoxy-6-quinolinecarboxamide or
     an analog thereof can be used in combination with a substance having a c-kit
     kinase-inhibiting activity to produce an excellent anti-tumor effect. For
     example, the effect of combination of 4-(3-Chloro-4-
     (cyclopropylaminocarbonyl)aminophenoxy)-7 -methoxy-6-quinolinecarboxamide
     methanesulfonate and imatinib on human gastrointestinal stromal tumor cell
     (GIST882 cell)-bearing model mice was examined
ΙT
     417716-92-8, 4-[3-Chlcoro-4-
     (cvclopropylaminocarbonyl)aminophenoxyl-7-methoxy-6-quinolinecarboxamide
     417717-05-6, 4-[3-Chlcoro-4-
     (cyclopropylaminocarbonyl)aminophenoxy]-7-(2-methoxyethoxy)-6-
     quinolinecarboxamide 417717-07-8,
     4-[3-Chloro-4-(cyclopropylaminocarbonyl)aminophenoxy]-7-[2-(4-
     morpholino)ethoxy-6-quinolinecarboxamide 417717-10-3,
     4-(3-Chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-(2-
     hydroxyethoxy)-6-quinolinecarboxamide 417717-15-8,
     4-(3-Chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-[(2S)-2,3-
     dihydroxypropyl)oxy-6-quinolinecarboxamide 417717-22-7,
     N6-Cyclopropy1-4-(3-chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-
     methoxy-6-quinolinecarboxamide 417717-23-8,
     N6-(2-Methoxyethyl)-4-(3-chloro-4-
     [[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-6-
     quinolinecarboxamide 417717-35-2,
     N6-(2-Hydroxyethyl)-4-(3-chloro-4-
     [[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-6-
     quinolinecarboxamide 417717-41-0,
     N6-(2-Fluoroethyl)-4-(3-chloro-4-
     [[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-6-
     quinolinecarboxamide 417717-44-3,
     N6-Methoxy-4-(3-chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-
     methoxy-6-quinolinecarboxamide 417717-76-1,
     N6-Methyl-4-(3-chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-
     methoxy-6-quinolinecarboxamide 417717-77-2,
     N6-Ethyl-4-(3-chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-
     methoxy-6-quinolinecarboxamide 417718-41-3,
     N-[2-Fluoro-4-[(6-carbamoy1-7-methoxy-4-quinoly1)oxy]pheny1]-N'-
     cyclopropylurea 417719-21-2,
     4-(3-Fluoro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-(2-
     methoxyethoxy)-6-quinolinecarboxamide 417719-50-7,
     4-[3-Chloro-4-(cis-2-fluoro-cyclopropylaminocarbonyl)aminophenoxy]-7-
     methoxy-6-quinolinecarboxamide 417719-56-3,
     4-(3-Chloro-4-(cyclopropylaminocarbonyl) aminophenoxy) -7-(2-ethoxyethoxy) 6-
     quinolinecarboxamide 417719-77-8,
```

RN 417717-05-6 HCAPLUS
CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-(2-methoxyethoxy)- (CA
INDEX NAME)

```
RN 417717-07-8 HCAPLUS
CN 6-Quinolinecarboxamide, 4-[3-chloro-4-
[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-[2-(4-morpholinyl)ethoxy]-
(CA INDEX NAME)
```

RN 417717-15-8 HCAPLUS
CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-[(2S)-2,3-dihydroxypropoxy](CA INDEX NAME)

Absolute stereochemistry.

RN 417717-22-7 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-N-cyclopropyl-7-methoxy- (CA INDEX NAME)

RN 417717-23-8 HCAPLUS
CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

 $\label{locality} \begin{tabular}{ll} [(\mbox{oyclopropylamino})\mbox{carbonyl}] \mbox{amino}] phenoxy] -7-methoxy-N-(2-methoxyethyl)-(CA INDEX NAME) \end{tabular}$

RN 417717-35-2 HCAPLUS

CN

6-Quinolinecarboxamide, 4-[3-chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-N-(2-hydroxyethyl)-7-methoxy-(CA INDEX NAME)

RN 417717-41-0 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-N-(2-fluoroethyl)-7-methoxy(CA INDEX NAME)

RN 417717-44-3 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-N,7-dimethoxy- (CA INDEX NAME)

RN 417717-76-1 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

RN 417717-77-2 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

[[(cyclopropylamino)carbonyl]amino]phenoxy]-N-ethyl-7-methoxy- (CA INDEX NAME)

RN 417718-41-3 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[4-[[(cyclopropylamino)carbonyl]amino]-3-fluorophenoxy]-7-methoxy- (CA INDEX NAME)

RN 417719-21-2 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[4-[[(cyclopropylamino)carbonyl]amino]-3-fluorophenoxy]-7-(2-methoxyethoxy)- (CA INDEX NAME)

RN 417719-50-7 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-[[[[(1R,2S)-2-fluorocyclopropyl]amino]carbonyl]amino]phenoxy]-7-methoxy-, rel- (CA INDEX NAME)

Relative stereochemistry.

$$\begin{array}{c} \text{MeO} \\ \text{H2N} \\ \end{array}$$

RN 417719-56-3 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-(2-ethoxyethoxy)- (CA INDEX NAME)

RN 417719-77-8 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-[(2R)-2-hydroxy-3-(1pyrrolidinyl)propoxy]- (CA INDEX NAME)

Absolute stereochemistry.

RN 417719-84-7 HCAPLUS

CN 6-Quinolinecarboxamide, N-(2-cyanoethyl)-4-[4-[[(cyclopropylamino)carbonyl]amino]-3-fluorophenoxy]-7-methoxy- (CA INDEX NAME)

RN 417720-85-5 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-(2-methoxyethoxy)-N-methyl(CA INDEX NAME)

RN 857890-39-2 HCAPLUS
CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-, methanesulfonate
(1:1) (CA INDEX NAME)

CM 1

CRN 417716-92-8
CMF C21 H19 C1 N4 O4

CM 2

CRN 75-75-2

CMF C H4 03 S

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REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 8 OF 23 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2007:150229 HCAPLUS Full-text

DOCUMENT NUMBER: 146:221063

TITLE: Method for assaying anti-tumor effect of angiogenesis

inhibitor

INVENTOR(S): Uenaka, Toshimitsu; Yamamoto, Yuji; Matsui, Junji

PATENT ASSIGNEE(S): Eisai R & D Management Co., Ltd., Japan

SOURCE: PCT Int. Appl., 147pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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PATENT NO.
                   KIND DATE APPLICATION NO. DATE
                       ____
    WO 2007015578
                       A1 20070208 WO 2006-JP315698 20060802
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
            KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,
            MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU,
             SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG,
            US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
            CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
            GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
    EP 1925676
                        A1 20080528
                                        EP 2006-768437
                                                                 20060802
        R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL,
            BA, HR, MK, RS
                                           JP 2005-224173 A 20050802
JP 2006-164700 A 20060614
PRIORITY APPLN. INFO.:
                                           WO 2006-JP315698 W 20060802
                       MARPAT 146:221063
OTHER SOURCE(S):
     Disclosed is a method for predicting the anti-tumor effect of an angiogenesis
AΒ
     inhibitor. The method comprises evaluating the EGF-dependence property of an
     angiogenesis inhibitor with respect to proliferation and/or survival of tumor
     cells, and using the evaluated EGF-dependence property as a measure. The
     anti-tumor effect of an angiogenesis inhibitor correlates with the EGF-
     dependency property of the inhibitor with respect to proliferation and/or
     survival of tumor cells. Therefore, an angiogenesis inhibitor is capable of
     exerting an excellent anti-tumor effect by using it in combination with a
     substance having an EGF inhibitory effect.
     417716-92-8, 4-(3-Chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-
     7-methoxy-6-quinolinecarboxamide 417716-92-80,
     4-(3-Chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-
    quinolinecarboxamide, pharmacol. allowed salt, solvate 417717-05-6
     , 4-(3-Chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-
    methoxyethoxy)-6-quinolinecarboxamide 417717-07-8
     417717-10-3 417717-15-8 417717-22-7
     417717-23-8 417717-35-2 417717-41-0
     417717-44-3 417717-76-1 417717-77-2
     417718-41-3 417719-21-2 417719-50-7
     417719-56-3 417719-77-8 417719-84-7
     417720-85-5 857890-39-2
     RL: ANT (Analyte); BSU (Biological study, unclassified); THU (Therapeutic
     use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
        (method for assaying anti-tumor effect of angiogenesis inhibitor by
       evaluating EGF-dependency)
    417716-92-8 HCAPLUS
RN
     6-Quinolinecarboxamide, 4-[3-chloro-4-
CN
     [[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy- (CA INDEX NAME)
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RN 417716-92-8 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy- (CA INDEX NAME)

RN 417717-05-6 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-(2-methoxyethoxy)- (CA INDEX NAME)

RN 417717-07-8 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylaminolcarbonyllaminolphenoxyl-7-[2-(4-morpholis

[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-[2-(4-morpholinyl)ethoxy]-(CA INDEX NAME)

RN 417717-10-3 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-(2-hydroxyethoxy)- (CA

INDEX NAME)

RN 417717-15-8 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-[(2S)-2,3-dihydroxypropoxy]-(CA INDEX NAME)

Absolute stereochemistry.

RN 417717-22-7 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

 $\label{local_condition} $$ [(\mbox{cylopropyl-7-methoxy-} \mbox{CA INDEX NAME})$$

RN 417717-23-8 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-N-(2-methoxyethyl)(CA INDEX NAME)

RN 417717-35-2 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-N-(2-hydroxyethyl)-7-methoxy(CA INDEX NAME)

RN 417717-41-0 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-N-(2-fluoroethyl)-7-methoxy-(CA INDEX NAME)

RN 417717-44-3 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

[[(cyclopropylamino)carbonyl]amino]phenoxy]-N,7-dimethoxy- (CA INDEX NAME)

RN 417717-76-1 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

 $\label{eq:condition} \begin{tabular}{ll} $[(cyclopropylamino)carbonyl]=mino]phenoxy]-7-methoxy-N-methyl- & (CA INDEX NAME) \\ \end{tabular}$

RN 417717-77-2 HCAPLUS CN 6-Quinolinecarboxami

CN 6-Quinolinecarboxamide, 4-[3-chloro-4[[(cyclopropylamino)carbonyl]amino]phenoxy]-N-ethyl-7-methoxy- (CA INDEX NAME)

RN 417718-41-3 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[4-[[(cyclopropylamino)carbonyl]amino]-3-fluorophenoxy]-7-methoxy- (CA INDEX NAME)

RN 417719-21-2 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[4-[[(cyclopropylamino)carbonyl]amino]-3-fluorophenoxy]-7-(2-methoxyethoxy)- (CA INDEX NAME)

RN 417719-50-7 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-[[[[(1R,2S)-2fluorocyclopropyl]amino]carbonyl]amino]phenoxy]-7-methoxy-, rel- (CA INDEX NAME)

Relative stereochemistry.

RN 417719-56-3 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-(2-ethoxyethoxy)- (CA INDEX NAME)

RN 417719-77-8 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-[(2R)-2-hydroxy-3-(1-pyrrolidinyl)propoxy]- (CA INDEX NAME)

Absolute stereochemistry.

RN 417719-84-7 HCAPLUS

CN 6-Quinolinecarboxamide, N-(2-cyanoethyl)-4-[4-[[(cyclopropylamino)carbonyl]amino]-3-fluorophenoxy]-7-methoxy- (CA INDEX NAME)

RN 417720-85-5 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4 [[(cyclopropylamino)carbonyl]amino]phenoxy]-7-(2-methoxyethoxy)-N-methyl (CA INDEX NAME)

RN 857890-39-2 HCAPLUS

CN 6-Quinolinecarboxamide, 4-[3-chloro-4-

[[(cyclopropylamino)carbonyl]amino]phenoxy]-7-methoxy-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 417716-92-8

CMF C21 H19 C1 N4 O4

CM 2

CRN 75-75-2 CMF C H4 O3 S

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2009 ACS on STN 2005:583343 HCAPLUS Full-text ACCESSION NUMBER:

DOCUMENT NUMBER: 143:248650

TITLE: Synthesis of Morphiceptin (Tyr-Pro-Phe-Pro-NH2) by Dipeptidyl Aminopeptidase IV Derived from Aspergillus

oryzae

AUTHOR(S): Ota, Toru; Itoh, Aki; Tachi, Hiroshi; Kudoh, Keita;

Watanabe, Tatsuo; Yamamoto, Yuji; Tadokoro,

Tadahiro; Maekawa, Akio

CORPORATE SOURCE: Department of Human Life and Development, Nayoro City

College, Nayoro, Hokkaido, 096-8641, Japan

SOURCE: Journal of Agricultural and Food Chemistry (2005),

53(15), 6112-6116

CODEN: JAFCAU; ISSN: 0021-8561 American Chemical Society

PUBLISHER: DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 143:248650

Morphiceptin (H-Tyr-Pro-Phe-Pro-NH2) was synthesized using dipeptidyl aminopeptidase IV (DPIV, EC 3.4.14.5; derived from Aspergillus oryzae RIB 915) as a peptide coupling catalyst. H-Tyr-Pro-OEt HCl was incubated with H-Phe-Pro-NH2·HC1 in the presence of DPIV under various conditions of temperature, concns. of ethylene glycol, pH, and reaction time. Morphiceptin was obtained at 40% yield under the optimal reaction conditions: substrates, 4 mM H-Tyr-

Pro-OEt:HCl and 20 mM H-Phe-Pro-NH2:HCl; enzyme, DPIV, 0.275 nkat; solvent, 60% ethylene glycol containing 20 mM phosphate buffer at pH 7.0; 4.2 mM diisopropylamine at 4° for 24 h. Amino group protection was unnecessary for this enzymic synthesis of morphiceptin.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2005:529441 HCAPLUS Full-text

DOCUMENT NUMBER: 143:278018

TITLE: Recent progress of angiogenesis inhibitors

AUTHOR(S): Watanabe, Tatsuo; Tsuruoka, Akihiko

CORPORATE SOURCE: Clinical Research Center, New Product Development Dep., Eisai Co., Ltd., Bunkyo-ku, Tokyo, 112-8088,

Japan

SOURCE: Saibo (2005), 37(4), 156-159

CODEN: SAIBC7; ISSN: 1346-7557

A review, discussing recent progress of angiogenesis inhibitors as antitumor

PUBLISHER: Nyu Saiensusha

DOCUMENT TYPE: Journal; General Review

LANGUAGE:

AB

Japanese

agents by targeting VEGF and its receptors.

L23 ANSWER 11 OF 23 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2005:374114 HCAPLUS Full-text DOCUMENT NUMBER: 143:33629

TITLE: K0 photoproduction on 12C in the threshold region AUTHOR(S): Watanaba, T.; Endo, S.; Fujii, Y.; Hashimoto, O.;

Watanabe, T.; Endo, S.; Fujli, Y.; Hashimoto, O.; Hirose, K.; Ishikawa, T.; Ito, K.; Kanda, H.; Katoh, M.; Kinoshita, T.; Konno, O.; Maeda, K.; Matsumura, A.; Miura, Y.; Miyahara, F.; Miyase, H.; Mizunuma, K.; Nakabayashi, T.; Nakamura, S. N.; Nomura, H.; Okayasu, Y.; Osaka, T.; Otani, A.; Oyamada, M.; Sasaki, A.; Sato, T.; Shimizu, H.; Takahashi, T.; Tamae, T.; Tamura, H.; Terasawa, T.; Tsubota, H.; Tsukada, K.; Ukai, M.; Utoyama, M.; Wakamatsu, M.; Yamauchi, H.;

Yamaguchi, Y.; Yamamoto, Y.; Yamazaki, H.

CORPORATE SOURCE: Department of Physics, Tohoku University, Sendai, 980-8578, Japan

SOURCE: Nuclear Physics A (2005), A754, 327c-331c

CODEN: NUPABL; ISSN: 0375-9474

PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The $\gamma n \to K0\Lambda$ process plays an important role in the study of strangeness production by the electromagnetic interaction. We have investigated the quasi-free production reaction on a 12C target in the threshold region (E γ = 0.8-1.1 GeV) at the Laboratory of Nuclear Science, Tohoku University.

Preliminary results are presented.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 12 OF 23 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2003:20255 HCAPLUS Full-text DOCUMENT NUMBER: 138:113464

TITLE: Photoproduction of neutral kaons on carbon in the

threshold region

Takahashi, T.; Watanabe, T.; Tsukada, K.; Kanda, H.; AUTHOR(S): Itoh, K.; Wakamatsu, M.; Yamazaki, H.; Kinoshita, T.; Ukai, M.; Osaka, T.; Mizunuma, K.; Yamamoto, Y.; Tamae, T.; Nakamura, S. N.; Fujii, Y.; Maeda, K.; Miyase, H.; Tsubota, H.; Tamura, H.; Kato, M.; Konno, O.; Sasaki, A.; Terasawa, T.; Hashimoto, O. CORPORATE SOURCE: Dep. Phys., Tohoku Univ., Sendai, 980-8578, Japan SOURCE: Kakuriken Kenkyu Hokoku (Tohoku Daigaku) (2002), 35, 30-33 CODEN: TLNRBV; ISSN: 0385-2105 PUBLISHER: Tohoku Daigaku Daigakuin Rigaku Kenkyuka Fuzoku Genshikaku Rigaku Kenkyu Shisetsu DOCUMENT TYPE: Journal LANGUAGE: English New data of the photoprodn. of the different iso-spin channels or spins AB observable are required. This proj. aims to measure γ + n \rightarrow K0 + Λ channel at the threshold region. As a 1st step of the expts., quasi-free production on C were measured. The present status of the spectrometer and anal. are reported on. The K0 is measured by detecting and reconstructing, K0s $\rightarrow \pi$ + + π - decay with the NKS (Neutral Kaon Spectrometer). The horizontal momentum of charged particles is determined by reconstructing the trajectory using the SDC (Straw Drift Chamber) and CDC (Cylindrical Drift Chamber) and Inverse of the velocity vs. momentum of the charged tracks. THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 4 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT L23 ANSWER 13 OF 23 HCAPLUS COPYRIGHT 2009 ACS on STN 2002:859508 HCAPLUS Full-text ACCESSION NUMBER: DOCUMENT NUMBER: 138:378719 TITLE: Sulfonamide derivative, E7820, is a unique angiogenesis inhibitor suppressing an expression of integrin $\alpha 2$ subunit on endothelium AUTHOR(S): Funahashi, Yasuhiro; Sugi, Naoko Hata; Semba, Taro; Yamamoto, Yuji; Hamaoka, Shinichi; Tsukahara-Tamai, Naoko; Ozawa, Yoichi; Tsuruoka, Akihiko; Nara, Kazumasa; Takahashi, Keiko; Okabe, Tadashi; Kamata, Junichi; Owa, Takashi; Ueda, Norihiro; Haneda, Toru; Yonaga, Masahiro; Yoshimatsu, Kentaro; Wakabayashi, Toshiaki CORPORATE SOURCE: Tsukuba Research Laboratories, Eisai Co., Ltd., Ibaraki, 300-2635, Japan Cancer Research (2002), 62(21), 6116-6123 SOURCE: CODEN: CNREA8: ISSN: 0008-5472 PUBLISHER: American Association for Cancer Research Journal DOCUMENT TYPE: LANGUAGE: English In the process of angiogenesis, endothelial adhesion mols. play a significant role in vascular morphogenesis, in coordination with angiogenic factor signaling. Here we report that a novel angiogenesis inhibitor, E7820 (an aromatic sulfonamide derivative), inhibited in vitro proliferation and tube formation of human umbilical vascular endothelial cell (HUVEC). E7820 decreased integrin $\alpha 2$, 3, 5, and $\beta 1$ in confluent culture of HUVEC, and

signaling. Here we report that a novel angiogenesis inhibitor, E7820 (an aromatic sulfonamide derivative), inhibited in vitro proliferation and tube formation of human umbilical vascular endothelial cell (HUVEC). E7820 decreased integrin $\alpha 2$, 3, 5, and $\beta 1$ in confluent culture of HUVEC, and integrin $\alpha 2$ was initially suppressed in mRNA level, followed by decrement of integrins $\alpha 3$, 5, and $\beta 1$. The inhibition of integrin $\alpha 2$ expression in HUVEC showed dose dependence but did not alter the level of CD31. Up-regulation of integrin $\alpha 2$ by phorbol 12-myristate 13-acetate abrogated the inhibitory effect of E7820 on tube formation within type I collagen gel, whereas addition of

antibody against integrin $\alpha 2$ canceled the phorbol 12-myristate 13-acetate effect. These results suggest that E7820 inhibited tube formation through the suppression of integrin $\alpha 2$. Oral administration of E7820 remarkably resulted in inhibition of tumor-induced angiogenesis in mouse dorsal air sac model, and tumor growth of human colorectal tumor cell lines (WiDr and LoVo) was inhibited in xenotransplanted model in mice. This is the first time that a small mol. has been shown to modulate integrins, and this finding may provide the basis for a new approach to antiangiogenic therapy through the suppression of integrin $\alpha 2$ on endothelium.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2001:581738 HCAPLUS <u>Full-text</u>

DOCUMENT NUMBER: 135:175421

TITLE: Integrin expression inhibitors

INVENTOR(S): Wakabayashi, Toshiaki; Funahashi, Yasuhiro; Hata, Naoko; Semba, Taro; Yamamoto, Yuji; Haneda, Toru; Owa, Takashi; Tsuruoka, Akihiko; Kamata, Junichi;

Okabe, Tadashi; Takahashi, Keiko; Nara, Kazumasa;

Hamaoka, Shinichi; Ueda, Norihiro

PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan

SOURCE: PCT Int. Appl., 153 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PA:	TENT	NO.			KIND DATE			APPLICATION NO.						DATE			
WO											2001 20 RU		3			20010	201
		AT,	,	CH,	,	,	,	,	,		,	,	IE,	IT,	LU	J, MC,	NL,
CA	2399	001			A1		2001	0809		CA	2001	-2399	001			20010	201
AU	2001	0288	67		A		2001	0814		AU	2001	-2886	7		20010201		
AU	781506				В2		2005	0526									
EP	1258252				A1		2002	1120	EP 2001-948941							20010	201
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GF	R, IT	, LI,	LU,	NL,	SI	E, MC,	PT,
		ΙE,	FI,	CY,	TR												
HU	2003	0005	44		A2		2003	0728		HU	2003	-544				20010	201
	2003						2005	0329									
NΖ	5202	99			A		2004	0528		NZ	2001	-5202	99			20010	201
RU	2240	826			C2		2004	1127		RU	2002	-1235	80			20010	201
CN	1003	5697	9		С		2007	1226		CN	2001	-8043	88			20010	201
JP	4039	856			В2		2008	0130		JΡ	2001	-5565	05			20010	201
US	2004	0018	192		A1		2004	0129		US	2002	-1815	62			20020	718
MX	2002	0072	49		Α		2002	1209				-7249				20020	725
KR	7670	00			В1		2007	1015		KR	2002	-7099	45			20020	801
NO	2002	0036	88		Α		2002	1003		ИО	2002	-3688				20020	802
US	2005	0176	712		A1		2005	0811		US	2005	-9721	8			20050	404
KR	7670	02			В1		2007	1015		KR	2007	-7017	61			20070	124
ORIT:	APP	LN.	INFO	.:						JΡ	2000	-2608	0		Α	20000	203
										JΡ	2000	-4020	84		Α	20001	.228
										WO	2001	-JP71	3		W	20010	201
												-1815				20020	-
										KR	2002	-7099	45		AЗ	20020	801

OTHER SOURCE(S): MARPAT 135:175421

AB Integrin expression inhibitors and remedies for arteriosclerosis, psoriasis, cancer, retinal angiogenesis, diabetic retinitis or inflammatory diseases, anticoagulant agents and cancerous metastasis inhibitors based on the integrin inhibitory effect. Namely, integrin expression inhibitors containing as the active ingredient sulfonamide compds. represented by the following general formula BKSO2N(R1)ZR, pharmacol. acceptable salts thereof or hydrates of the same wherein B represents optionally substituted C6-10 aryl or 6- to 10-membered heteroaryl wherein the ring may be partly saturated; K represents a single bond, -CH=CH- or -(CR4bR5b)mb- (wherein R4b and R5b may be the same or different and each represents hydrogen or C1-4 alkyl; and mb represents an integer of 1 or 2); R1 represents hydrogen or C1-6 alkyl; Z represents a single bond or CO-NH-; and R represents optionally substituted C6-10 aryl or 6- to 10-membered heteroaryl wherein the ring may be partly saturated

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2001:563144 HCAPLUS $\underline{\text{Full-text}}$

DOCUMENT NUMBER: 135:283445

TITLE: Mice lacking histidine decarboxylase exhibit abnormal

mast cells

AUTHOR(S): Ohtsu, H.; Tanaka, S.; Terui, T.; Hori, Y.;

Makabe-Kobayashi, Y.; Pejler, G.; Tchougounova, E.; Hellman, L.; Gertsenstein, M.; Hirasawa, N.; Sakurai, E.; Buzas, E.; Kovacs, P.; Csaba, G.; Kittel, A.; Okada, M.; Hara, M.; Mar, L.; Numayama-Tsuruta, K.; Ishigaki-Suzuki, S.; Ohuchi, K.; Ichikawa, A.; Falus,

A.; Watanabe, T.; Nagy, A.

CORPORATE SOURCE: Department of Cellular Pharmacology, Tohoku University

School of Medicine, Aoba-ku, Sendai, 980-8575, Japan

SOURCE: FEBS Letters (2001), 502(1,2), 53-56

CODEN: FEBLAL; ISSN: 0014-5793

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal LANGUAGE: English

AB Histidine decarboxylase (HDC) synthesizes histamine from histidine in mammals. To evaluate the role of histamine, we generated HDC-deficient mice using a gene targeting method. The mice showed a histamine deficiency and lacked histamine-synthesizing activity from histidine. These HDC-deficient mice are viable and fertile but exhibit a decrease in the nos. of mast cells while the remaining mast cells show an altered morphol. and reduced granular content. The amts. of mast cell granular proteases were tremendously reduced. The HDC-deficient mice provide a unique and promising model for studying the role of histamine in a broad range of normal and disease processes.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 16 OF 23 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2001:489373 HCAPLUS Full-text

DOCUMENT NUMBER: 135:76882

TITLE: Preparation of heterocyclic compounds having

sulfonamide groups as inhibitors of angiogenesis
INVENTOR(S): Haneda, Toru; Tsuruoka, Akihiko; Kamata, Junichi;
Okabe, Tadashi; Takahashi, Keiko; Nara, Kazumasa;
Hamaoka, Shinichi; Ueda, Norihiro; Wakabayashi,

Toshiaki; Funahashi, Yasuhiro; Semba, Taro; Hata, Naoko; Yamamoto, Yuji; Ozawa, Yoichi; Tsukahara,

Naoko; Owa, Takashi

PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan SOURCE: PCT Int. Appl., 94 pp.

JOURGE: FCI IIIC. App

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

GI

PA.	TENT	NO.	KIND DATE			APPLICATION NO.							DATE					
WO								WO 2000-JP9326 NO, NZ, RU, US							20001227			
		AT,		CH,	CY,		DK,							IE,	IT,	LU	, MC,	NL,
CA	2395	772			A1		2001	0705		CA	20	000-	2395	772		:	20001	227
AU	2001	0222	83		A		2001											
AU	AU 776933						2004	0923										
EP	1243	583			A1		2002	0925		ΕP	20	000-	9859	53		:	20001	227
EP	1243	583			В1		2005	0928										
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GI	R,	ΙT,	LI,	LU,	NL,	SE,	, MC,	PT,
		ΙE,																
	2002						2003			HU	2(002-	3973			:	20001	227
	2002						2004											
	5193						2004	1029									20001	
	2239						2004							15			20001	
	1217						2005							05			20001	
AT	3053	02			Τ		2005							53			20001	
	2246						2006							53			20001	
	4234						2009							63			20001	
	2003						2003			US	20	002-	1492	53		- 2	20020	610
	6787						2004											
	3242						2007			ИО	20	002-	3097			- 3	20020	
	2002				A		2002	1129		MX	20	002-	6474			_	20020	
PRIORIT	Y APP	LN.	INFO	.:													19991	
														26		W :	20001	227
OTHER SO	OTHER SOURCE(S):						CASREACT 135:76882; MARPAT 135:76882											

$$B-K-\bigvee_{y}^{Q}-\bigvee_{h}^{R_{1}}\bigvee_{z}^{X}\bigvee_{y}^{Y}\bigvee_{b}^{T}$$

AB Heterocyclic compds. having sulfonamide or sulfonylurea groups, specifically heterocyclic compds. of general formula (I), pharmacol. acceptable salts of the same, or hydrates of both [wherein A is hydrogen, halogeno, optionally halogenated C1-4 alkyl, hydroxy, cyano, (CO)kNR2R3, or optionally substituted C2-4 alkenyl or alkynyl (wherein R2 and R3 are each independently hydrogen or optionally halogenated C1-4 alkyl; k is 0 or 1); B is optionally substituted aryl, monocyclic heteroaryl, or Q1 (wherein the ring Q is an optionally substituted aromatic ring containing 1 or 2 N atoms; the ring M is optionally substituted and unsatd. C5-12 monocyclic or polycyclic ring sharing a double

bond with the ring Q and optionally containing 1-4 heteroatom selected from N, O, and S; the ring Q and M may share a N atom); K is a single bond or (CR4R5)m (wherein R4 and R5 are each independently hydrogen or C1-4 alkyl; m is 1 or 2); T, W, X and Y are each independently =C(D) - (wherein D is hydrogen, halogeno, hydroxy, C1-4 alkyl, halo-C1-4 alkyl, or the like) or nitrogen; U and V are each independently =C(D)-, nitrogen, oxygen, or CO; Z is a single bond or -CONH-; and R1 is hydrogen or C1-4 alkyl] are prepared These compds. includes N-quinolinylpyridinesulfonamides, N-quinolinylbenzenesulfonamides, Nquinolinylquinolinesulfonamides, N-quinolinylindolinesulfonamides, Nquinolinylisoquinolinesulfonamides, N-quinolinylbenzofuransulfonamides, Nquinolinyltetrahydronaphthalanesulfonamides, Nquinolinylbenzoxathiansulfonamide, N-quinolinylbenzothiopyransulfonamide, Nisoquinolinylpyridinesulfonamides, N-isoquinolinylbenzenesulfonamides, Nnaphthyridinylpyridinesulfonamides, N-naphthyridinylbenzenesulfonamides, Nquinolinylpyridazinesulfonamides, etc. They are useful as therapeutics based on angiogenesis inhibition such as antitumor agents, cancer metastasis inhibitors, and therapeutics for diabetic retinopathy, rheumatic arthritis, and hemangioma. Thus, 5-indansulfonyl chloride was added to a solution of 3amino-8-bromoquinoline in pyridine and stirred at room temperature for 30 min to give N-(8-bromoquinolin-3-y1)-5-indansulfonamide (II). II and <math>N-(8-bromoquinolin-3-y1)bromoquinolin-3-yl)-6-methoxypyridazine-3-sulfonamide in vitro showed IC50 of 0.04 and 0.53 ug/mL, resp., against angiogenesis in rat aorta.

THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 41 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2000:608721 HCAPLUS Full-text

DOCUMENT NUMBER: 133:193071

TITLE: Preparation of sulfonamide-containing indole

derivatives as inhibitors of neovascularization and

tumor

Haneda, Toru; Tsurucka, Akihiko; Kamata, Junichi; INVENTOR(S): Okabe, Tadashi; Takahashi, Keiko; Nara, Kazumasa; Hamaoka, Shinichi; Ueda, Norihiro; Ohwa, Takashi;

Wakabayashi, Toshiaki; Funahashi, Yasuhiro; Semba, Taro; Hata, Naoko; Yamamoto, Yuji; Ozawa, Yoichi;

Tsukahara, Naoko

PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan; et al.

SOURCE: PCT Int. Appl., 44 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA:	IENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO	2000050395 W: AU, CA,	A1 CN, HU, JE		WO 2000-JP1071 NO, NZ, RU, US	20000224
				FI, FR, GB, GR, IE, I	T, LU, MC, NL,
	PT, SE				
JP	2000247949	A	20000912	JP 1999-49870	19990226
CA	2327253	A1	20000831	CA 2000-2327253	20000224
CA	2327253	C	20071016		
EP	1074542	A1	20010207	EP 2000-905321	20000224
EP	1074542	B1	20060503		
			, ES, FR,	GB, GR, IT, LI, LU, N	L, SE, MC, PT,
CA EP	2327253 1074542 1074542	C A1 B1 CH, DE, DE	20071016 20010207 20060503	EP 2000-905321	20000224

HU	2001001434	A2	20010928	HU	2001-1434		20000224
HU	2001001434	A3	20011029				
RU	2208607	C2	20030720	RU	2000-129508		20000224
AU	766936	B2	20031023	AU	2000-26916		20000224
NZ	507464	A	20031031	NZ	2000-507464		20000224
CN	1132814	C	20031231	CN	2000-800229		20000224
AT	325094	T	20060615	AT	2000-905321		20000224
ES	2259997	Т3	20061101	ES	2000-905321		20000224
JP .	3866041	B2	20070110	JΡ	2000-600978		20000224
US	6469043	B1	20021022	US	2000-647215		20000928
XM	2000010243	A	20010410	MΧ	2000-10243		20001019
ИО .	2000005357	A	20001222	NO	2000-5357		20001024
ИО .	317299	В1	20041004				
US .	20020128480	A1	20020912	US	2002-98420		20020318
US	6673787	В2	20040106				
US .	20020128483	A1	20020912	US	2002-98421		20020318
US	6638964	В2	20031028				
JP	2006312652	A	20061116	JP	2006-226414		20060823
PRIORITY	APPLN. INFO.:			JP	1999-49870	Α	19990226
				JP	2000-600978	АЗ	20000224
				WO	2000-JP1071	W	20000224
				US	2000-647215	АЗ	20000928

OTHER SOURCE(S): MARPAT 133:193071

GΙ

AB The title compds. I [R1 represents hydrogen, etc.; R2 and R3 are the same or different and each represents hydrogen, etc.; R4 represents hydrogen or lower (C1-4) alkyl; and the ring A represents cyanophenyl, etc., provided that the following cases are excluded: the one where R1, R2 and R3 are all hydrogen atoms; the one where R2 and R3 are both hydrogen atoms; and the one where the ring A is an aminosulfonylphenyl group and R1 and R2 are both halogen atoms; and provided that when the ring A is a cyanophenyl, 2-amino-5-pyridyl or 2-halogeno-5-pyridyl group and R1 is a cyano group or a halogen atom, then at least one of R2 and R3 is not hydrogen] are prepared The title compound II in vitro showed IC50 of 10 μq/mL against mouse B16 melanoma cells.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 18 OF 23 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 1999:746753 HCAPLUS Full-text

DOCUMENT NUMBER: 132:88701

TITLE: Involvement of the histaminergic system in leptin-induced suppression of food intake

AUTHOR(S): Morimoto, T.; Yamamoto, Y.; Mobarakeh, J. I.; Yanai,

K.; Watanabe, T.; Watanabe, T.; Yamatodani, A.

CORPORATE SOURCE: Faculty of Medicine, School of Allied Health Sciences,

Department of Medical Physics, Osaka University,

Suita, Osaka, Japan

SOURCE: Physiology & Behavior (1999), 67(5), 679-683

CODEN: PHBHA4; ISSN: 0031-9384

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal LANGUAGE: English

LANGUAGE: English

AB The ob gene product leptin is secreted from white adipose tissue, and may regulate food intake by acting on the hypothalamus in the central nervous system. But the mechanism of this effect is still unclear. The central histaminergic system has been suggested to participate in the control of

various physiol. functions, particularly in feeding behavior, as it mediates anorectic signals like leptin. Thus, the authors hypothesized that the central histaminergic system is a target for leptin in its control of feeding. To prove this, the authors first examined the effect of i.p. administration of lpha-fluoromethylhistidine (FMH), a specific and irreversible inhibitor of histidine decarboxylase, on leptin-induced suppression of food intake in normal C57BL strain mice. Leptin treatment (1.3 mg/kg, i.p.) significantly reduced food intake by 60% of that of control at 6 h and by 84% at 24 h compared with control. When mice were injected with FMH (100 mg/kg, i.p.) before being given leptin, leptin-induced suppression of food intake was abolished and there was no significant difference compared with that of control. Addnl., the authors further examined the effects of leptin on food intake in mutant mice lacking histamine H1 receptors (H1R-KO mice). Leptin injection significantly reduced food intake by 56% of that of control at 6 h and by 79% at 24 h in wild-type mice (WT mice), but not in H1R-KO mice. This finding suggests that leptin affects the feeding behavior through activation

of the central histaminergic system via histamine H1 receptors.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 1996:420261 HCAPLUS <u>Full-text</u>

DOCUMENT NUMBER: 125:84454

ORIGINAL REFERENCE NO.: 125:15926h,15927a

TITLE: Human monoclonal rheumatoid factors augment arthritis

in mice by the activation of T cells

AUTHOR(S): Ezaki, I.; Okada, M.; Yoshikawa, Y.; Fujikawa, Y.;

Hashimoto, M.; Otsuka, M.; Nomura, T.; Yamamoto, K.;

Watanabe, T.; et al.

CORPORATE SOURCE: Medical Institute Bioregulation, Kyushu University,

Oita, 874, Japan

SOURCE: Clinical and Experimental Immunology (1996), 104(3),

474-482

CODEN: CEXIAL; ISSN: 0009-9104

PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English

In order to investigate the in vivo role of rheumatoid factor (RF), the AB effects of the administration of human monoclonal (m) IgM-RF and IgG-RF on the development of arthritis in mice were examined The administration of human mRFs into mice immunized with type II collagen (CII) markedly enhanced the clin. score and paw swelling. The severity of arthritic joint disease with a marked infiltration of lymphoid cells, proliferation of synovial membrane, pannus formation and destruction of articular cartilage was significantly enhanced in both groups receiving RF (RF-enhanced arthritis). Skin ulcers were also observed in some of these RF-enhanced arthritis mice, whereas no such signs were observed in CII-immunized mice without mRFs. Both IqM-RF and IgG-RF increased CII-specific IgG antibodies in circulation, and the severity of arthritis correlated with the production of high titers of anti-CII antibodies. In vivo treatment of RF-enhanced arthritis mice with an anti-CD4 MoAb or an anti-CD8 MoAb inhibited the induction and progression of arthritis in these mice. Administration of RF to severe combined immunodeficient (SCID) mice with arthritis developed by the transfer of spleen cells from CIIimmunized mice, prolonged the arthritis and enhanced the severity. This murine model of RF-enhanced arthritis may provide a useful tool for analyzing the pathogenesis of rheumatoid arthritis in RF-pos. patients.

L23 ANSWER 20 OF 23 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 1987:56343 HCAPLUS $\underline{\text{Full-text}}$

DOCUMENT NUMBER: 106:56343

ORIGINAL REFERENCE NO.: 106:9223a,9226a

TITLE: Heat capacities and adsorption energies of helium adsorbed on Y zeolites with various cations
AUTHOR(S): Wada, N.; Yamamoto, Y.; Kato, H.; Ito, T.;

Watanabe, T.

CORPORATE SOURCE: Fac. Sci., Hokkaido Univ., Sapporo, 060, Japan SOURCE: Studies in Surface Science and Catalysis (1986),

28 (New Dev. Zeolite Sci. Technol.), 625-32

CODEN: SSCTDM; ISSN: 0167-2991

DOCUMENT TYPE: Journal LANGUAGE: English

AB Influence of an elec. field of cation on He-adsorbed on Y zeolite and its motional state were studied by measuring the heat capacities and adsorption isotherms. The localization potential, W, that is van der Waals potential-enhanced by the elec. field to localize He near the cation, was estimated to be W(Ca2+)/k > 170 K, W(Na+)/k .apprx.28 K, and W(H+)/k <6 K. An isosteric heat of sorption obtained from the present adsorption isotherm has a very large temperature dependence in comparison with that assuming a classical oscillation or translation of the He adatom. This dependence may suggest discrete energy levels of the motional state due to a quantum effect confined into a small pore of diameter .apprx.10 Å.

L23 ANSWER 21 OF 23 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 1986:609267 HCAPLUS $\underline{\text{Full-text}}$

DOCUMENT NUMBER: 105:209267

ORIGINAL REFERENCE NO.: 105:33755a,33758a

TITLE: Absolute configuration at C-24 of 5β -ranol, a

principal bile alcohol of the bullfrog

AUTHOR(S): Kihira, K.; Noma, Y.; Tsuda, K.; Watanaba, T.;

Yamamoto, Y.; Une, M.; Hoshita, T.

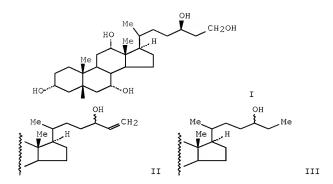
CORPORATE SOURCE: Sch. Med., Hiroshima Univ., Hiroshima, 734, Japan

SOURCE: Journal of Lipid Research (1986), 27(4), 393-7

CODEN: JLPRAW; ISSN: 0022-2275

DOCUMENT TYPE: Journal LANGUAGE: English

GΙ



AB The stereochem, of the hydroxyl group at C-24 in 5β -ranol (I), a principal bile alc. of the bullfrog which is structurally related to a major human urinary bile alc., was described. Cholestenetetrols II were synthesized from cholic acid by the condensation of 24-aldehyde with vinylmagnesium bromide. The absolute configurations at C-24 of II were elucidated by means of the difference of the reactivity to Sharpless oxidation, a stereoselective epoxidn. Catalytic hydrogenation of II yielded tetrols III. Alternatively, III were prepared from norcholestanic acid by a Kolbe electrolytic coupling with acetic acid. The LiAlH4 reduction of the norcholestanic acid provided I.

L23 ANSWER 22 OF 23 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 1984:163571 HCAPLUS Full-text

DOCUMENT NUMBER: 100:163571

ORIGINAL REFERENCE NO.: 100:24809a,24812a

TITLE: Experimental progress in plasma dynamics and

generation of energetic particles in dense plasma

focus

AUTHOR(S): Yokohama, M.; Kitagawa, Y.; Yamada, Y.; Okada, M.;

Yamamoto, Y.; Yamanaka, C.; Hirano, K.; Kondoh, Y.;

Shimoda, K.; et al.

CORPORATE SOURCE: Inst. Laser Eng., Osaka Univ., Suita, Japan

SOURCE: Plasma Physics and Controlled Nuclear Fusion Research

(1983), Volume Date 1982, 9th(2), 415-24

CODEN: PPCRDU; ISSN: 0589-1469

DOCUMENT TYPE: Journal

LANGUAGE: English

The progress of recent expts. in dense plasma focus is described. Correlation AB between macroscopic behavior of focused plasma and n yield in 2 Mather-type devices, A and B, are presented. A Filippov-type device, C, was used to observe plasma dynamics including current sheet, imploding and reflected shock wave. In device A, nuclear activation is used for measuring d intensity,

energy spectrum and angular distribution. Cellulose nitrate particle-track detectors are used for high-energy p. Spatial and temporal locations of generation of high-energy ions are observed by ruby laser holog. interferometry. Ion pinhole cameras are used for determining the localization of high-energy ion generation. Energetic ions are produced and accelerated by a plasma diode. Ion temps. in focused plasma are estimated from measurement of the D-D/D-3He reaction ratios in a D2-3He mixture gas experiment. In the upstream and downstream directions with resp. to the discharge current, e and ion beams were observed in device B. The n were generated by a moving plasma diode mechanism. According to the measurement performed with a multiframing interferometer for device C, the highest collapse of the current sheet was attained at the collision between the collapsing current sheet and the related shock wave.

L23 ANSWER 23 OF 23 HCAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 1983:23857 HCAPLUS Full-text

DOCUMENT NUMBER: 98:23857
ORIGINAL REFERENCE NO.: 98:3667a,3670a

TITLE: Light ion beams generation in dense plasma focus AUTHOR(S): Yokoyama, M.; Kitagawa, Y.; Yamada, Y.; Okada, M.;

Yamamoto, Y.; Hori, T.; Yamanaka, C.

CORPORATE SOURCE: Inst. Laser Eng., Osaka Univ., Suita, 565, Japan SOURCE: Res. Rep. - Nagova Univ., Inst. Plasma Phys. (1982),

Res. Rep. - Nagoya Univ., Inst. Plasma Phys. (1982), IPPJ-611, Proc. Int. Top. Meet. ICF Res. Light - Ion

Beam, 35-9

CODEN: NIPRAL; ISSN: 0469-4732

DOCUMENT TYPE: Report LANGUAGE: English

AB High-energy d and p in a Mather-type plasma-focus device were measured by nuclear activation techniques. Radioactivity induced in graphite, Al, and Cu targets provided the d intensity, energy spectrum, and angular dependence. The high-energy p were measured by cellulose nitrate particle track detectors. The energy spectrum of d and p had 2 components and a mean d energy of 1.55 MeV under the low pressure mode and 1.44 MeV under the high pressure mode, resp. The angular distribution of the d beam was .ltorsim.30° under the low pressure mode. Under the high pressure mode, distribution showed multistructure, and 2 peaks were observed at .ltorsim.20 and .apprx.60°, resp., which may be due to the azimuthal rotation of the d around the axis.

=> d his nofile

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L4
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